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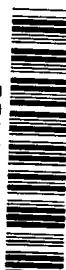


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THE EFFECT OF SPACE-FLIGHT FACTORS ON FUNCTIONS OF THE CENTRAL NERVOUS SYSTEM

N. N. Livshits, Editor-in-Chief

"Nauka" Izdatel'stvo, Moscow, 1966



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THE EFFECT OF SPACE-FLIGHT FACTORS ON FUNCTIONS
OF THE CENTRAL NERVOUS SYSTEM

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Translation of "Vliyaniye faktorov kosmicheskogo poleta na
funktsii tsentral'noy nervnoy sistemy."
Izdatel'stvo "Nauka," Moscow, 1966

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SOME PROBLEMS OF THE EFFECTS OF SPACE-FLIGHT FACTORS
ON THE CENTRAL NERVOUS SYSTEM

N. N. Livshits

The present report, written by specialists of a space biology section /3* of the Institute of Biological Physics, USSR Academy of Sciences, is a continuation of an earlier publication, "Effect of Ionizing Radiations and Dynamic Factors on Functions of the Central Nervous System" (Vliyaniye ioniziruyushchikh izlucheniye i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy).

This collection of articles reflects the further development of experimental investigations of the effect of vibration, accelerations, and ionizing radiations on some functions and metabolism of the central nervous system (CNS) and cerebral hemodynamics.

The problem of the effect of vibration on the central nervous system has been comprehensively studied by many authors (Andreyeva-Galanina, 1956; Andreyeva-Galanina et al., 1961; Drogichina et al., 1961; Mel'kumova, 1960; Shpil'berg, 1964; Borshchevskiy et al., 1963, and others). However, problems related to the effects of this factor can by no means be considered as completely resolved.

In particular, further studies of the quantitative patterns and mechanisms of the reactions of the nervous system to repeated exposure to vibration are of great importance in elucidating the possible adaptation of the organism to the effects of unusual irritants.

These problems are considered in articles by L. D. Luk'yanova et al., and M. A. Kuznetsova (this report). These authors investigated the development of adaptation to vertical vibration with a frequency of 70 cps, amplitude of 0.4 mm, and duration of 15 min, and studied the course of recovery after termination. Studies by L. D. Luk'yanova and others were based on an integrated approach which included measurement of metabolic processes, recording fast and slow forms of bioelectric activity in different parts of the brain, and investigation of conditioned reflexes. This made it not only possible to elucidate the dynamics of the processes investigated, but to also postulate their possible mechanisms.

In earlier studies (Luk'yanova, 1964b) it was discovered that vibrations caused two-phase changes in metabolic processes of cerebral tissues. /4 During vibration the rate of oxygen consumption increased while at the end of

*Numbers given in margin indicate pagination in original foreign text.

exposure to or after vibration, this reaction was replaced by a depression of metabolic processes.

Investigations published in this collection show that after multiple exposure to vibration there was a lengthening of the phase of metabolic stimulation (Luk'yanova et al.). In rats subjected to prior destruction of the middle ear or otoliths, the phase of metabolic depression was not observed when it was clearly manifested in intact animals (L.D. Luk'yanova and S. M. Ambrosova). The authors hypothesized that the reason for these changes of vibration effects is limitation of peripheral impulsation to the higher parts of the brain. In the first case this limitation of impulsation was caused by a general decrease in cortical excitability, while in the second, by partial surgical destruction of receptors. This hypothesis is confirmed by the chronic depression of bioelectric activity in the cortex and subcortical formations of rats exposed to vibration.

At the same time, joint investigations of conditioned reflexes, bioelectric activity of the brain, and metabolic processes (L. D. Luk'yanova et al.) and observations of the dynamics of changes in the characteristics of the unconditioned defensive reflex (M. A. Kuznetsova), revealed an incompleteness of adaptation and that it occurs as a result of sharp functional changes in the CNS.

The difficulty and incompleteness of adaptation to the effects of vibration was manifested clearly in an investigation of their effect on the unconditioned motor defense reflexes of guinea pigs. During the course of tenfold exposure to vibration a successive change of parabiogenic phases in the spinal reflex arc took place indicating a transition from a deeper to a less deep state of inhibition. However, complete normalization of unconditioned reflex activity was not attained (M. A. Kuznetsova).

These observations show that exposure to vibration, even in small doses, far less than those which can cause vibration sickness, is a strong CNS irritant. These findings agree well with numerous references in the literature (Andreyeva-Galanina, 1956, 1963; Andreyeva-Galanina, Drogichina et al., 1961; Borshchevskiy et al., 1963, and others) and the results of our earlier studies. M. A. Kuznetsova (1964a) demonstrated that double exposure to vibration with the cited parameters changes the basic characteristics of the unconditioned ¹⁵ motor defense reflex in the guinea pig to an equal degree as lethal, whole-body gamma irradiation. Additional information on the effect of vibration on the CNS is given in articles by M. A. Kuznetsova, N. N. Livshits and Ye. S. Meyzerov. In these studies it is confirmed that vibrations with the indicated parameters have an inhibitory effect on higher and lower nervous activity.

In an investigation of conditioned reflexes, this is manifested in the form of protective inhibition while in unconditioned reflex activity, it is characterized by parabiogenic phases. Inhibition of CNS functions during vibration is characteristic of most animals, but the intensity of these reactions and the form they take depends on individual characteristics. During vibrations the latent periods of spinal reflexes increased in some animals without disruption of force ratios, while in others there occurred equilibrium or paradoxical phases or an intermediate stimulus phase.

The inhibition of conditioned reflex activity in some rats during vibrations took the form of a temporary total disappearance of conditioned reflexes, while in others these reflexes merely declined in strength.

Disruptions of proper force ratios in some cases took the form of a low level adjustment phase, while in others, a total ultraparadoxical phase.

At the same time, in an animal in a state of protective inhibition, the effect of vibration caused disinhibition of conditioned reflexes. The results of our experiments confirm the opinion of many authors who believe that vibrations act on higher nervous activity in the form of an unconditioned inhibition (Gurovskiy, 1959, and others). However, at the same time comparison of the effect of noise, the classical agent causing unconditioned inhibition, with that of vibration-noise irritant shows an appreciable difference between the effects of these factors. The effect of vibration is considerably stronger, has a more generalized character, and attenuates more slowly.

A characteristic feature of vibration effects is the duration of the aftereffect period.

In earlier studies (Apanasenko, 1964a; Kuznetsova, 1964a) it was demonstrated that after twofold vibration with the above-mentioned parameters, changes of the motor defense and vestibular-tonic reflexes were maintained for more than 10-15 days.

Prolonged postvibration changes in the bioelectric activity of different parts of the brain and conditioned and unconditioned reflexes after single and multiple exposures to vibration were demonstrated in the articles by Luk'yanova et al., M. A. Kuznetsova and N. N. Livshits and Ye. S. Meyzerov. Investigations of the functions of different parts of the CNS using different methods give results which are in complete agreement, indicating their general character.

The article by Z. I. Apanasenko very clearly describes the characteristics of the effect of vibration and acceleration. She compared the effect of three factors on resting bioelectric activity of the extensor muscles of an extremity and on the vestibular-tonic reflexes in guinea pigs. These included space-flight, twofold (one day interval) 15-min centrifugation with an acceleration of 8 g in a "back-chest" direction, and double exposure to vibration with the same duration. The author was thus able to determine the characteristics of the effect of combined factors as well as the role of each component in space-flight effects. It was found that accelerations cause substantial but brief changes in the functions investigated; the changes caused by vibration are more moderate, but at the same time, more persistent. All enumerated experimental results indicate that among the complex of dynamic factors which occur during active phases of a space flight, lift-off vibrations are of considerable significance and must be considered.

Dynamic factors not only affect CNS functions, but also affect its reactions to irradiation.

The articles devoted to the combined effect of vibration and irradiation on the functions of the vestibular apparatus (Z. I. Apanasenko) and conditioned

reflex activity (N. N. Livshits and Ye. S. Meyzerov) are a continuation of reports published in the preceding collection of articles. It was earlier demonstrated that preliminary or preliminary and subsequent exposure to vibration can appreciably change the effect of lethal, whole-body irradiation on some CNS functions. Different types of reactions were discovered in these investigations. Vibration prior to whole-body gamma irradiation exerted a protective effect on oxidation processes in cerebral tissues. Despite the fact that irradiation and the effect of vibration caused depression of oxidation processes, there was no summation of their effects when both factors were simultaneous, and in some cases the effect of combined exposure to both was less than the effect of irradiation alone (Luk'yanova, 1964c). The results of the experiments of L. D. Luk'yanova agree with the data of M. A. Arsen'yeva (cited in Frank et al., 1965) and Yu S. Demin (1964), indicating that disruptions of mitotic activity in cell nuclei of the hematopoietic system during combined exposure to these factors, also are not cumulative and that vibration sometimes exerts an obvious protective effect.

However, the combined effect of vibration and irradiation on the functions of the CNS is more complex. In an investigation of the combined effect of vibration and lethal gamma irradiation on unconditioned defense reflexes, the bioelectric activity of the muscles during relative rest and vestibular- tonic reflexes to adequate stimulation of the otolithic part of the vestibular apparatus, various changes in radiation reactions characterized by a dominance of one factor or by their combined effects were found (Apanasenko, 1964b; Kuznetsova, 1964b).

In a study by N. N. Livshits and Ye. S. Meyzerov, published in this collection, it was demonstrated that under the influence of vibration and subsequent whole-body irradiation in a dose of 50 r conditioned reflex changes in the course of the first week duplicated the vibration effect in all its details. In the second week, there was a not entirely clear trend toward summation and combination of the effects of both factors.

The dominance of the vibration effect in the initial period after irradiation was noted earlier in an investigation of the combined effect of vibration and acute irradiation in a dose of 500-600 r on the intensity of oxidation processes in cerebral tissues (Luk'yanova, 1964c) and on the functional state of the vestibular apparatus (Apanasenko, 1964b). Similar effects are described by Z. I. Apanasenko for a combination of the effect of vibration and prolonged irradiation (p. 217).

We can now state that such a reaction to a combined effect is characteristic of both higher and lower parts of the CNS. It applies for a combination of vibration and irradiations in different doses and with different rates of application of these factors. At the same time, it should be remembered that this form of reaction is not the only possible one. Following combined exposure to vibration and irradiations, changes in the unconditioned defense reflexes of some groups of animals were dominated during the entire period of observation by vibration effects, whereas in other groups the effects of irradiation were dominant (Kuznetsova, 1964b). /7

The combination of the effect of both factors was also observed earlier in the second phase of the reaction of the lower parts of the CNS to combined factors. These effects are extremely complex, and do not fit the scheme which assigns a protective role to the dynamic factor (Apanasenko and Kuznetsova, 1964; Apanasenko, 1964b; Kuznetsova, 1964b).

The combined effect changed the background bioelectric activity of the muscles in the same way as vibration, and the dynamics of these changes corresponded to those irradiated animals. Since in some cases there was a 8 mutual intensification of the effects of both factors in those periods when they were weak and mutual attenuation when they were strong, we postulated the participation of the mechanisms of parabiosis and dominants in these phenomena (Livshits, 1964). However, this explanation is not applicable to the results of the experiments of N. N. Livshits and Ye. S. Meyzerov. Beginning with the second exposure, there was total summation of the effects of radiation and dynamic factors, regardless of their intensity. This compels us to assume the presence of mechanisms which intensify the radiation reaction of the higher parts of the CNS upon repeated exposure to vibration with subsequent irradiation, and which mask the possible protective effect of depression of oxidation processes.

Besides the combined effect of ionizing radiations and dynamic factors, in developing the problem of radiation safety in space flight it is of interest to consider the problem of the dependence of radiation reactions on the CNS on the factors of time and the type of radiation.

The CNS, as pointed out in our earlier studies (Apanasenko, 1961; Kuznetsova, 1961; Livshits et al., 1962), reacts to a change of the dose intensity in a unique fashion and differs in this respect from many other organs and systems of the animal body.

In most cases a decrease in the rate of exposure during irradiation in sublethal and minimum lethal doses does not modify the effect of radiation on the functions of the CNS. Slightly increased effectiveness of chronic irradiation compared to acute irradiation in equal doses was not statistically reliable based on earlier data. However, additional experiments revealed that a one-month exposure to whole-body gamma irradiation (160 r) disrupts conditioned reflex activity in rats more dramatically than the same irradiation of only two minutes duration. The slight differences in basic indices of the higher nervous activity between groups subjected to chronic and brief irradiation were statistically reliable (Ye. S. Meyzerov, this report).

The important role of the functional state of the vestibular analyzer in the sense of well-being and work capacity of a cosmonaut served as the basis for special investigations of the dependence of the reactions of this system to irradiation on the dose intensity. Here, a comparison was made of the effect of whole-body irradiation (600 r) with exposure durations of 14 hr and about 2 min. No modification of radiation reaction as a function of a decrease in dose intensity was observed in this case. On the basis of several indices, qualitative differences characterized by a different trend or different dynamics

of changes were noted. For example, the bioelectric activity of muscles upon adequate stimulation of the otolithic part of the vestibular apparatus decreased during chronic irradiation, whereas during a brief exposure it increased. The scatter of data was considerably less for animals exposed to chronic irradiation. /9

The duration of aftereffects decreased during exposure to both forms of irradiation, but the effect of chronic irradiation was stronger.

During combined exposure to vibration and chronic irradiation, the effect of radiation was found to be stronger than a combination of vibration and acute irradiation. In the former case the "contribution" of radiation to the total effect was greater (Z. I. Apanasenko, in this report).

Contrary to reactions of the nervous system, changes in the cellular composition of the peripheral blood were greater during acute irradiation, in the studies of Ye. S. Meyzerov and Z. I. Apanasenko which agree with the literature. Z. I. Apanasenko also noted an obvious decrease in mortality during chronic irradiation.

In analyzing the mechanism of the effect of irradiation on CNS functions, it is of great importance to clarify the effect of this factor on cerebral circulation.

According to Lyubimova-Gerasimova, 1962, this system is relatively radio-resistant; consequently, V. Ya. Klimovitskiy (this report) studied whole-body and local irradiations in doses of 1000 and 2000 r, respectively. Even in the first hours after exposure, cerebral venous circulation had clearly decreased. However, despite the fact that such intense doses were used, differences between experimental and control rabbits were not consistently reliable and the significance level did not exceed 5 percent, which indicates that cerebral circulation is relatively radioresistant. It can therefore be assumed that subtle functional changes in the CNS during irradiation in small doses are not of vascular origin.

Three articles by A. P. Korolevskiy are devoted to the peculiarities of the effect of different kinds of radiation on the higher nervous activity. Presently this subject has not yet been treated in the literature despite its obvious importance. A comparison of the effects of whole-body irradiation with 1 MeV

neutrons, 510 MeV protons and Co^{60} gamma radiation in lethal and sublethal doses on drinking conditioned reflexes of mice and rats revealed a parallelism between the dependence of higher CNS radiation reactions on much studied hematopoietic reactions relative to the type of radiation. The RBE of 510 MeV protons is less than one while for fast neutrons it is greater than one where the CNS and blood of small animals are concerned. The author describes the qualitative characteristics of the effect of these types of radiation on the conditioned reflexes. In the case of exposure to protons a disruption of the inhibition process is more characteristic, whereas in animals irradiated by neutrons, modification of excitation is most evident. In all probability this /10

difference is related to the lesser RBE of protons. In animals irradiated by neutrons in doses used by the author, protective inhibition was extremely evident. However, it was coupled with internal inhibition, which masked the possible attenuation of the latter. To a lesser degree this was also true of animals exposed to gamma irradiation. A detailed analysis of the mechanism of this phenomenon in irradiated animals was first offered by A. V. Lebedinskiy and Z. N. Nakhil'nitskaya (1960).

Neutrons do not play a significant role in the biological effect of space radiation, but investigations of the characteristics of their effect on the animal's body are of definite interest. To clarify the general problem of the dependence of CNS reactions on the type of radiation, it would be desirable to compare three (rather than two) types of irradiations as a function of variable linear ionization density.

These studies have considered some of the possible characteristics of the effect of ionizing radiations under space-flight conditions: different dose rates, change in radiation spectrum, combined effects of radiation and dynamic factors. These factors all exert a substantial effect on CNS functions. In addition, dynamic factors clearly alter the metabolism and functions of the CNS. The data presented here indicate the desirability of continuing research in this direction.

These problems are also germane to terrestrial occupational hygiene.

EFFECT OF RADIAL ACCELERATIONS ON THE BRAIN TEMPERATURE OF ANIMALS

V. Ya. Klimovitskiy

ABSTRACT

Temperature under the dura mater was recorded in one dog and six rabbits exposed to radial accelerations on a centrifuge. Temperatures were measured with thermistors to within $3.0 \cdot 10^{-3}$ degrees.

Longitudinal and transverse directions were studied. The animals were exposed to repeated daily accelerations of 10 g for 30 sec with 30-min intervals.

In rabbits, longitudinal accelerations caused an acute decrease in temperature with an immediate return to normal after stopping. In the dog the analogous temperature peak was directed upward. After repeated exposures the degree of the reaction first increased and then decreased. This phenomenon can be interpreted as initial adaptation.

During transverse accelerations there was a temperature increase of small variability in the dog and rabbit.

In most cases, after the end of rotation there was a slow decrease of temperature with a return to normal after 15-20 min.

The observed temperature changes are compared with those induced by an increase of inhaled carbon dioxide. The results also are compared with data on cerebral circulation under the same conditions.

Recently researchers have been investigating the heat production of the brain as one of the integral characteristics of its functional state. /11

Despite the simplicity of determining this parameter through modern methods and its obvious scientific and practical importance, there still remain many gaps in this area of study.

In considering brain temperature as an "index of its functional state" (Berezovskiy, 1963), it is usually assumed that the specific activity of neurons has a corresponding thermal expression, e.g., the excitation process is accompanied by an increase of heat production. The experimental verification of this hypothesis is complicated by the fact that the active state of a part of

the brain, apparently even an individual neuron, is associated with increased circulation (Klosovski, 1951).

There is no uniformity of opinion relative to factors most responsible for determining changes in local brain temperatures. There are two opposite points of view on this subject; one holds that the local temperature of the brain is primarily dependent on the level of functional activity, the second holds that the temperature index is basically a function of circulation. These two approaches divide researchers in this field into two camps (Berezovski, 1963).

Such disagreements can possibly be attributed to the fact that the simplicity of temperature measurements, even when using modern miniaturized sensors (thermistors, thermocouples), is only apparent. The precise measurement of local temperatures in the living body is quite complex and demands very clearly defined methodology. For example, it can be shown that temperature

measurement in a major artery to an accuracy of 10^{-2} degree by use of a thermocouple requires the introduction of the junction into the vessel. The 12 heat transfer along the leads of the thermocouple situated outside the artery makes it impossible to obtain a precise measurement of the temperature of the blood itself. In actuality, in the latter case we will measure the temperature of the adjoining tissue, and if this thermocouple is situated within a sleeve covering the vessel, it is the temperature of the latter which will be recorded.

The relationship between the temperatures of the blood and the brain has been established by different methods using different subjects. In 1954, working with thermistors, Ludwigs demonstrated that in dogs the surface structures of the brain are heated by the inflowing blood and the deep structures are cooled. Berezovski (1962, 1963), in measuring the temperature of the cortex with thermistors and the temperature of the blood by thermocouples outside the vessel, found that in dogs the temperature of the arterial blood is below the temperature of the surface of the hemispheres. Yu. N. Orestenko (1962) established that in rabbits the brain temperature is considerably lower than the temperature of the arterial blood.

The variety of facts obtained by Berezovski in the experiment on dogs makes it possible to distinguish between functional heat production of the brain and the general cortical temperature reaction observed in animals during excitation. The author observed a temperature increase in dogs in the motor region of the cortex, functionally related to the front extremity during passive bending of the paw or irritation of the extremity with an induction current. A temperature rise is also observed at the time of food or motor excitation. Usually, such a rise was preceded by a brief temperature decrease. The author attributes the latter to the initial intensification of circulation in the investigated region and, according to his data, cooling of this region by the blood.

In our experiments we undertook the problem of investigating the dynamics of changes in the brain temperature of animals multiply exposed to radial

accelerations in a "pelvis - head" and chest - back" direction. Earlier we obtained data on the state of the cerebral venous blood flow in rabbits under these conditions (Klimovitskiy, 1964b). As will be demonstrated below, comparison of these data with cerebral thermograms still does not make it possible to isolate heat production of the brain from heat transfer by the blood. In this report we will therefore limit ourselves to the phenomenology of this process and some hypotheses.

The experiment was conducted using six rabbits and one dog. The sensors, containing MT-54 thermistors, were placed in a trepanned opening 8 mm in diameter. Solid meninx was removed along the perimeter of the opening. The thermistors were inserted into the brain to a depth of 0.5 mm in the frontal and parietal regions. In some cases temperature was measured directly adjacent to the longitudinal venous sinus.

The thermistors operated in the arm of a dc bridge whose unbalance signal was fed to a dc amplifier. An N-373-2 instrument was used for recording. 13 The reading of temperatures on the tape of the automatic recorder was done with

an accuracy to $3.0 \cdot 10^{-3}$ degree. The thermistors were calibrated in an ultra-thermostat. The scale in ohms was established on the tape of the automatic recorder at the beginning and end of the experiment.

The animals were exposed to experimental conditions three to five days after the operation and were observed for up to a month. A month after the operation, the sensor was removed from the dog and replaced, after which the experiment was continued for another month.

An acute experiment was carried out on one rabbit. In addition to the temperature sensor a cannula with a thermistor was placed in the common carotid. In this case the operating part of the thermistor was situated at the entrance of the cannula, extending 0.5 mm into the blood flow. The operation was carried out under local anesthesia (heparin).

Animals were exposed to radial accelerations on a centrifuge. During longitudinal accelerations ("pelvis - head") a field of about 5 g was attained in the region of the head and 10 g in the region of the pelvis. During "chest - back" accelerations the animals were exposed to 10 g on a tilting transverse platform where the angular acceleration was directed in the "pelvis - head" direction. In both cases the operating time of the motor was 30 sec, which arbitrarily is assumed to be lower during the exposure time, although in actuality these 30 seconds also include the period of acceleration of the centrifuge (5 sec) while braking time (15 sec) is excluded.

The designations used in this study for the radial accelerations ("pelvis - head" and "chest - back") are not generally accepted in the biological literature, but they reflect the physical and not the apparent direction of the accelerations, which are centripetal. In many cases the opposite designation ("head - pelvis"), used in the Soviet literature, is erroneous. The longitudinal

accelerations used in our experiment also can be called "positive" (a term used more frequently in the foreign literature). In actuality, during longitudinal accelerations the animals were placed along the radius with the head toward the center of rotation, and on the transverse rotating platform--with the head in the direction of rotation.

At the time of the experiment the animals were covered with a plastic hood to prevent exposure to air currents during rotation. Air was fed under the hood for breathing purposes from the gas collector of the centrifuge and a scattering grid.

The animals were attached to the platform by means of very tightly secured coveralls. The head of the animal was held motionless during experiments with longitudinal accelerations. /14

EXPERIMENTAL RESULTS

In the first approximation, fluctuations in the temperature profile of the rabbit and dog are similar and can be classified into two groups according to frequency and amplitude. Within the limits of hundredths of a degree the fluctuations had a period of about tens of seconds (type I). The amplitudes of the slow temperature waves with a period of several minutes, sometimes tens of minutes, were tenths of a degree (type II). Berezovskiy gives a similar classification. We note that rapid fluctuations sometimes were absent, and the thermogram within the limits of resolution of our instruments appeared completely smooth. In this case there were only slow temperature waves--in the same animal type I fluctuations appeared and disappeared spontaneously on different days of the experiment. The preliminary reaction to an indifferent irritant in the dog was accompanied by a temperature increase of several hundredths of a degree; in the rabbit it developed as a result of strong irritants.

An increase in carbon dioxide content in the inhaled air (5-7 percent) for both the dog and rabbits caused a rapid rise of temperature by $0.1-0.2^{\circ}$. In the rabbit this was followed by a rapid, smooth decrease to below the initial level by almost a degree. Type I fluctuations were not considered in this part of the decline. In the dog, the maximum increase was followed by a slow return of the temperature to the initial level. Type I fluctuations were persistent against this background.

Longitudinal Accelerations. Thermogram During Acceleration

During accelerations in the "pelvis - head" direction the temperature at all points investigated dropped steeply in the case of the rabbit. After shutting off the motor and during gradual deceleration, there was occasionally a small peak apparent against a background of continuing decrease; the decrease then continued until complete stoppage of the centrifuge (fig. 1a; fig. 2b).

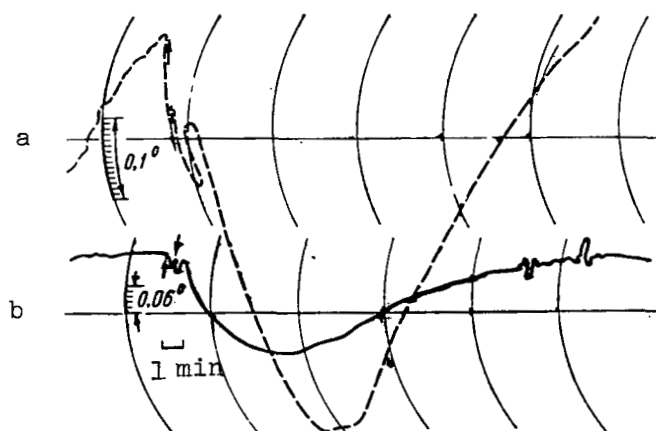


Figure 1. Thermogram from a thermistor in the parietal surface of the left cerebral hemisphere of a rabbit. a, second day of experiment; b, fifth day of experiment; arrows, starting and stopping of the motor.

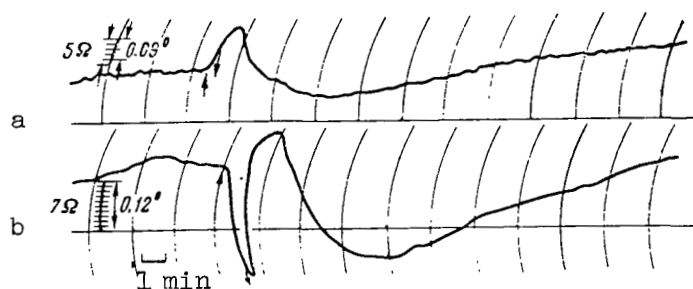


Figure 2. Rabbit thermogram. Parietal region. a, "chest - back" acceleration; b, "pelvis - head" acceleration.

The value of the initial decrease of temperature from the initial value on the first day of the experiment was $0.1-0.2^{\circ}$, increasing with the number of the accelerations. The maximum reaction was observed on the second day of the experiment, sometimes toward the end of the first day (above 0.2°). The reaction then decreased from day to day, and by the fourth or fifth day it became established within the limits of a somewhat stable minimum (fig. 1b). After an interruption of one or more days, the magnitude of the initial drop

again increased, but upon subsequent accelerations rapidly attained the same minimum value.

An essentially different picture was observed in the dog when the accelerations were longitudinal. During the initial exposure, on the first day of the experiment the starting of the motor was accompanied by a steep temperature increase. The lag in reaction relative to the start of the centrifuge (10 mm/min) was not determined. The increase on the first day was $0.1-0.15^{\circ}$. After complete stopping of the centrifuge the temperature dropped with equal intensity to below the initial level (fig. 3a). On the next day the initial temperature increase was less. At the same time, the duration of elevation increased after switching off the motor. The process of displacement of the initial increase

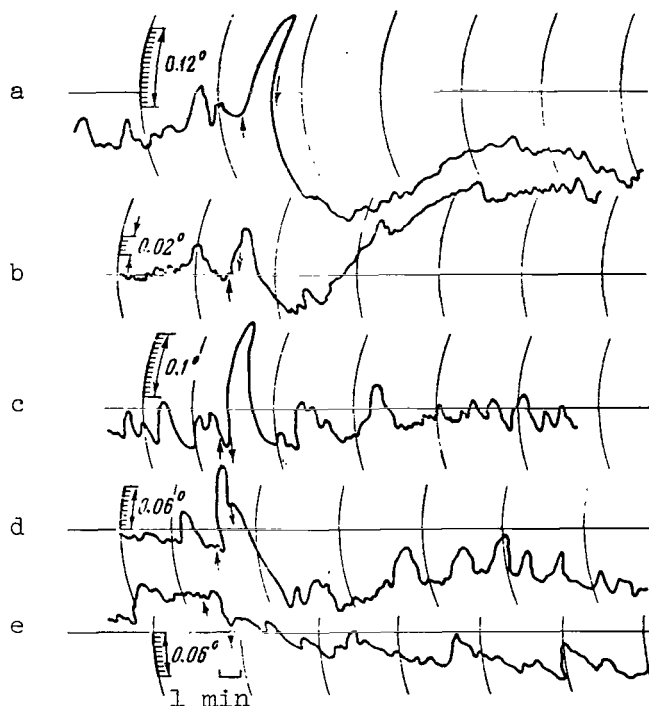


Figure 3. Thermogram of the frontal region of the brain cortex of a dog.

"Pelvis - head" acceleration.

a, first exposure, 30 sec, first day of experiment; b, first exposure, 30 sec, second day of experiment; c, first exposure, 30 sec, third day of experiment after a one-day interruption; d, fourth exposure, 30 sec, same day; e, fourth exposure, 60 sec, fourth day of experiment.

into the aftereffect phase began. This lag was intensified on the third day, when the entire initial peak developed only after switching off the motor (fig. 3c). Here, directly after switching on the motor, there was a small decrease in temperature, and only at the end of a 30-sec acceleration did an increase begin. It could be clearly seen that elevation increased with a decrease in rotation. Figure 3 also shows that on the second day the reaction was weaker than on the first. On the third day of the experiment, after a 1-day interruption, curve height again was restored to the initial level, but up on the fourth acceleration (fig. 3d) the height was less than that of the first acceleration of this same day. Thus, while the characteristics of the temperature reaction in the dog differed from the rabbit, the multiple effects of accelerations were completely identical. /17

It was characteristic that in the case of an increase in duration to 60 sec or more the first upward peak was completely absent, while for all practical purposes the temperature reaction to rotation of more than 30 sec was characterized by a brief decrease in temperature within the limits of type I thermal noise.

Finally, we note the disappearance of type I fluctuations during the development of the initial temperature reaction within the first days of the experiment. Immediately after the initial temperature peak the type I fluctuations are absent; then they are gradually restored, but with a lesser amplitude (fig. 3a). On subsequent days, type I fluctuations appear quickly upon completion of the initial phase of the reaction (figs. 3c, 3d). This pattern is clearly expressed on the dog and rabbit thermograms.

Transverse Accelerations. Thermogram During Acceleration

After switching on the motor the temperature at all investigated points increased, and this trend was sustained for some time after stopping the centrifuge (fig. 2a). In general, such a temperature change is characteristic of rabbits and the dog. The steepness of the peak is less and type I fluctuations are initially distinguishable and subsequently absent. The initial temperature change, relative the original level, was less than during longitudinal accelerations and for rabbits and the dog was 0.05-0.15°. The reaction was stable, with little variation. Its value fluctuated randomly and apparently was not related with the number of accelerations for either rabbits or the dog.

Aftereffect Reaction

The temperature changes after total stoppage of the centrifuge were the most unstable components of the reaction relative to total deviation, duration and trend.

After longitudinal acceleration, the rapid initial temperature peak for rabbits and the dog was followed by a smooth temperature decrease. Peak /18

duration on the first day of the experiment was 10-15 min. It was not possible to establish the precise time of reaction termination since during the final observations it was lost in spontaneous temperature fluctuations and is indistinguishable from type II fluctuations. The maximum temperature decrease for rabbits (fig. 4) and the dog was noted on the second day and thus coincides with the maximum value of the first phase. Later the steepness of the temperature decrease drops off generally duplicating the characteristic of the initial reaction. In the dog however, the magnitude and duration of aftereffects decrease far more rapidly than the magnitude of the initial reaction. Whereas the initial temperature peak was restored after a 1-day interruption, the aftereffect disappeared almost completely (figs. 3a, 3c) and apparently was not restored.

Aftereffect temperature changes in the rabbit were always constant (temperature decrease), regardless of acceleration vector. In the case of transverse accelerations, the reaction was stable in value and did not clearly depend on the number of exposures.

A considerable aftereffect temperature increase ($> 0.3^{\circ}$) was observed in the dog during the first exposure to transverse acceleration. On the following

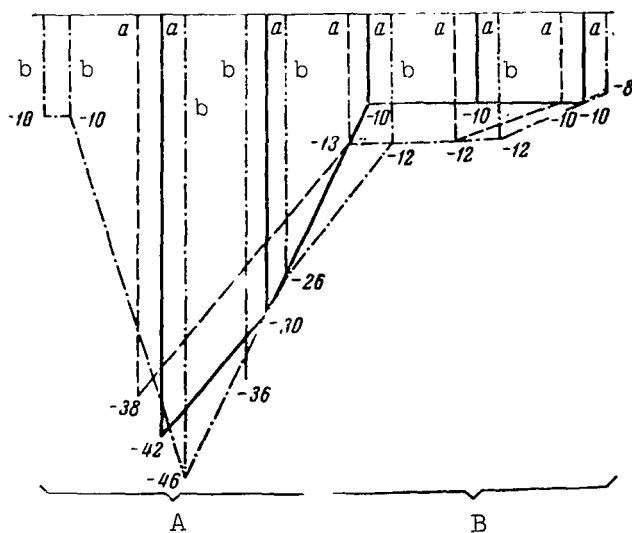


Figure 4. External values of the aftereffect reaction in rabbits from three brain surfaces. a, parietal region; b, frontal region; A, External during longitudinal accelerations after 3 days of experiment; B, same, for transverse accelerations. Figures--hundredths of a degree.

days the reaction decreased considerably, reached zero, reversed (decrease by 0.14°) and again returned to a positive value, but did not reach the initial value (fig. 5). At the same time, the height of the initial temperature peak remained the same during transverse accelerations.

Thus, the intensity of the aftereffect reaction in the rabbit was very obviously related to the magnitude of the initial reaction, whereas no such trend was observed in the dog.

Discussion

In generally accepting the hypothesis of most authors to the effect that there is a difference between the temperatures of inflowing blood and the brain, it can be asserted that the circulatory changes are undoubtedly reflected in the overall temperature reaction to acceleration.

The rapid component of temperature changes during longitudinal accelerations in the rabbit probably reflected changes in cerebral blood circulation. It is difficult to assume that metabolic processes, or more precisely, their thermal expression, change so rapidly and to such an extent as occurred in the first phase of the temperature reaction in the rabbit. The dynamics of these temperature changes observed during acceleration are definitely related to the effect of mechanical factors: the reaction begins and is intensified with the starting of the motor and rapidly ceases after the centrifuge is completely stopped.

Under these same conditions the cerebral thermogram for the dog essentially differs. First, the upward peak is the immediate result of longitudinal

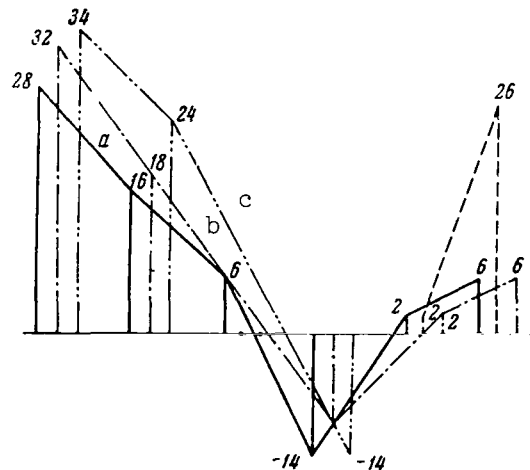


Figure 5. Extremal values of the aftereffect reaction in the dog. a, frontal region; b, c, parietal region.

acceleration during the first exposures. Second, this peak is completely unrelated to the beginning of the action of the mechanical factor and can be completely displaced into the aftereffect. Finally, with an increase in the operating duration of the motor (above 30 sec) the initial rise not only does not become greater, but may not occur at all. At the same time, with the lag of the temperature rise, a second component of this reaction, lesser in amplitude, occurs: a downward peak, definitely related to the beginning of the acceleration. Although for the time being we have no other data for a more complete analysis of these phenomena, we do intend to consider the first upward peak observed in the dog during longitudinal accelerations, also attributal to circulatory changes. However, whereas in our opinion the downward peak in the rabbit is the result of initial mechanical movement of blood, in the dog the upward peak possibly reflects compensatory changes in circulation. This does not mean that in the rabbit the initial reaction should remain constant as a function of the stability and reproducibility of the operating physical factor. The sequence of changes in venous blood circulation in rabbits during multiple exposure to longitudinal accelerations coincides completely with the described sequence of changes of the first phase of the temperature reaction under these conditions (Klimovitskiy, 1964b).

As pointed out, the magnitudes of the initial temperature reaction in the dog during longitudinal accelerations had a similar chronological development. These coincidences were not considered proof, but they clearly suggest that the primary temperature reaction in the dog and rabbit can be considered as hemodynamic.

In the light of the data cited in the literature on the temperature difference between the inflowing blood and the brain, it would be possible to explain the difference in the trends of the initial temperature changes in the dog and rabbit during longitudinal accelerations as follows: The temperature of the arterial blood in the dog is lower than brain temperature while in the rabbit it is higher. During "pelvis - head" accelerations cerebral anemia occurs. Therefore, the surface of the cerebral hemispheres of the brain of the dog is "heated" while in the rabbit it is "cooled," due to insufficient ^{/21} blood supply during acceleration. However, such a simple explanation is obviously inadequate. During longitudinal accelerations we always observed in the rabbit a phase of intensification of venous circulation. It must also be taken into account that the thermistors were placed in the bifurcations of the surface veins carrying blood of a different temperature than the temperature of the surface of the hemispheres; thus, according to these data, in the rabbit there was "cooling" while in the dog there was "heating." As we mentioned before, the increase in venous circulation is the end result of mechanical factors (loss of venous blood) and physiological compensation. Thus, the temperature in the region where the thermistor was placed in our case is a function of at least three variables: functional heat production of the brain, arterial inflow and venous outflow.

We did not investigate changes of blood circulation during transverse accelerations. On the basis of the literature (Henry et al., 1951) it should be expected that these changes will be less than during longitudinal accelerations.

The temperature changes were accordingly smaller. New data compared to the reaction to longitudinal accelerations indicate: (a) coincidence of the trend of the initial temperature peak for the rabbit and dog; (b) stability of the temperature reaction and its apparent nondependence on the number of exposures to the acceleration.

The insufficiency of blood supply to the brain is obviously accompanied by an increase in the concentration of carbon dioxide in cerebral tissues and cerebral blood. The latter via reflexes leads to compensatory vasodilatation. We compared the effect of an increased content of carbon dioxide in the inhaled air with the effect of accelerations. The external analogy of the temperature reaction to carbon dioxide and to transverse accelerations for the dog and rabbit was very close. The aftereffect of the reaction of blood circulation to carbon dioxide was similar to the aftereffect of the reaction to longitudinal accelerations for the rabbit. Without regarding these similarities as proof of the similarity of the mechanisms, we nevertheless consider the following interpretation to be applicable: Transverse accelerations create an initial inadequacy of blood supply accompanied by a deficit of oxygen and an excess concentration of carbon dioxide in cerebral tissues. This change in the gas balance leads to an increase in functional heat production. It was demonstrated that in the case of asphyxia and with total cessation of blood circulation, the brain temperature in dogs rises sharply (Berezovskiy, 1964). We observed a considerable terminal rise of temperature in rabbits during exposures to acute accelerations after total cessation of cerebral blood flow. It is known that asphyxia is accompanied by motor excitation, resulting in spasm. According to data in the literature, these phenomena are accompanied by a considerable /22 increase in functional heat production in the motor region of the hemispheres.

What we have stated makes it possible to consider the initial temperature increase during transverse accelerations as primarily functional and not hemodynamic. This, of course, does not solve the problem of the participation of circulatory changes in the formation of these thermal processes.

As mentioned above, there is a similarity in circulatory changes during recovery after exposure to longitudinal acceleration or an increased content of carbon dioxide. Specifically: in the period of the temperature minimum in the aftereffect the blood flow in the rabbits increased. At the time of gradual temperature recovery, the blood flow is normalized and becomes somewhat less than at rest. During all this time the temperature remains below the initial level. Thus, it would be possible to consider the temperature decrease in the aftereffect to be the result of decreased functional heat production, provided the temperature of the arriving blood is stable. However, this is not the case. In the acute experiment on the rabbit we recorded temperature changes in the carotid. It was demonstrated that with an increase in inhaled carbon dioxide content, the blood temperature in the carotid undergoes an initial two-phased change; the first peak is directed upward. In the aftereffect the temperature returns slowly to the initial level. Apparently, the role of the hemodynamic factor in the formation of aftereffect temperature reactions in the rabbit cannot be taken into account.

The temperature reactions in the dog during recovery after accelerations were more complex. We are presently unable to interpret them.

The measurement of the body temperature of animals exposed to accelerations has been recently conducted by a number of authors (Danileyko, 1964; Matsinin, 1964; Simeonova, 1964). In experiments on mice and rats after accelerations of 30-40 g for up to 3 min the authors observed a so-called "post-gravitational hypothermia." This phenomenon involved a decrease in rectal and surface temperature by 1-3°, lasting from 30 min to several hours. According to the observations made by Danileyko, similar temperature changes also occurred in the internal organs. The temperature of the internal organs was measured in animals killed immediately after rotation.

The temperature measurements in these investigations, insofar as can be judged from brief communications, were made with some methodological shortcomings. For example, it was difficult to avoid mechanical cooling of the experimental animals, when in the course of several minutes of acceleration they were exposed to air currents. The authors of this study attempted to avoid this complication by wrapping the animals. There is no basis for assuming that this measure was effective. Moreover, we feel that the conclusion that there is a temperature decrease in the internal organs on the basis of measurements on dead animals is unsound, even if death occurred 1-2 min prior to the temperature measurement. Thus, only data on a decrease in rectal temperature are absolutely reliable. This phenomenon, like the temperature decrease in the other investigated regions, is attributed by the authors to gravitational hypoxia, associated with hemodynamic and respiratory impairments. The duration and intensity of accelerations used in the studies cited were not comparable to those used in our study. However, as already mentioned, a brief and not intense hypothermal aftereffect occurred. Only initial transverse accelerations in the experiment with a dog yielded a considerable temperature increase during the aftereffect. /23

Conclusions

1. The temperature reaction of the brain to accelerations in the rabbit and dog was characterized by two distinct phases, the first of which is related to the duration of the mechanical effect and the second of which develops after its termination.

2. The first phase of the temperature reaction to longitudinal accelerations during a series of successive exposures undergoes changes similar to those in cerebral blood flow under these conditions and is a result of their physiological and mechanical effect.

3. The first phase of the temperature reaction to transverse accelerations differs from the similar phase for longitudinal accelerations in its stability and low dependence on the number of preceding exposures.

4. The aftereffect is a thermal expression of compensatory processes and is quantitatively related to the intensity of the temperature changes which occur during acceleration.

FUNCTIONAL STATE OF THE OTOLITHIC PART OF THE VESTIBULAR
ANALYZER OF GUINEA PIGS AFTER DOUBLE EXPOSURE
TO CENTRIFUGATION

Z. I. Apanasenko

ABSTRACT

The effect of double exposure to acceleration (chest-back, 8 g, 15 min, one day interval) and the functional state of the otolithic apparatus of the guinea pig were investigated. The change in some myoelectric characteristics of vestibular-tonic hind leg reflexes was noted. These changes are of a shorter duration and in some cases are of a lesser magnitude than those after vibration with similar parameters (vertical, 0.4 mm, 7 cps, twice for 15 min with a one day interval). A hypothesis on the mechanism of the observed effects is advanced.

The condition of the experimental animals revealed no departure from normal; analysis of the peripheral blood disclosed insignificant leukocytosis.

The effects of space flight, acceleration, and vibration are compared with respect to indices of the vestibular-tonic reflex. In some cases the effects of space flight reveal some cumulation of vibration and acceleration effects, although they were not fully reproducible.

Many investigations of the influence of accelerations on the animal and human body have been made in recent years in relation to advances in astronautics. Changes in pulse and respiration rates, blood pressure, tissue metabolism and physiological parameters were determined (Babushkin, 1959; Barer et al., 1963; Kotovskaya et al., 1962; Kovalenko et al., 1963; Fasser et al., 1963). Impairment of hemodynamics is of the greatest importance, especially under the influence of longitudinal accelerations; this impairment is the most significant of the many functional disturbances (Marukhanyan, 1961; Gazulov, 1955; Rosin et al., 1959; Usachev, 1961; Beckman et al., 1954). Among the deviations from normal in CNS activity are frequent cases of lengthening of the latent periods, disruption of the conditioned reflexes and disinhibition of differentiations (Barer, 1962a,b; Brestkin, 1958; Bronshteyn and Zagryadskiy, 1958; Vinogradov et al., 1953; Dmitriyev and Kotova, 1960, 1961; Kislyakov, 1956, 1958; Beckman et al., 1954). Stress reactions during exposure to accelerations are sometimes accompanied by slowing of psychomotor responses and deterioration of instantaneous memory and response to information processes (Chambers and Hitchcock, 1963).

In pharmacological (Belay, Vasil'yev and Kolchin, 1964) and electroencephalographic investigations (Barer, 1962; Barer et al., 1963; Izosimov and Razumeyev, 1960, 1962; Savin and Sulimo-Samuylio, 1960, 1958) it was discovered that exposure to accelerations causes impairment of the functional interrelations of stimulation and inhibition processes in the cortex and subcortex of the brain.

Under space flight conditions particularly high requirements are imposed on the activity of the vestibular apparatus, on which the feeling of well-being and the work capacity of cosmonauts are highly dependent. Naturally, for modern aviation and space science it is of very great importance to study these changes, which may arise in relation to the impairment of the vestibular functions under the influence of accelerations, which constitute a powerful dynamic factor in space flight. /26

One of the important changes is disruption of motor coordination. Some motor-coordination impairments (especially fine movements) were observed during or after exposure to accelerations by many investigators. V. S. Gurfinkel' and his coauthors (1959), in experiments in a high-speed elevator at Moscow State University (~ 2 g), noted that subjects experienced an increase in the body oscillation amplitudes and displacement of the hands from their regular position.

Impairment of coordination with an increase of amplitude and rhythm of movements was also observed during accelerations by B. M. Savin (1957). During accelerations of 3 and 7 g, the subjects were less able to differentiate the force of applied pressure (Chkhaidze, 1962a,b); at accelerations of 2-5 g there was impairment of the capacity to adequately evaluate a lifted weight (Marukhanyan et al., 1962). High accelerations of 20 g or more cause a still more significant discoordination of movements--trembling and involuntary movements of the torso and extremities (Rhein, Taylor, 1963; Bruce, Barr, 1963).

On the other hand, it can be considered established that an increase in acceleration (to a certain value) is accompanied by an increase in the amplitude of bioelectric currents in skeletal muscles (Babushkin et al., 1961; Barer, 1962a; Barer, Golov et al., 1963; Kotovskaya et al., 1962; Marukhanyan et al., 1962; Yuganov et al., 1963). At present it is usually assumed that increased bioelectric activity of the muscles is evidence of an increase in muscle tonus and is a compensatory mechanism accompanying the effect of accelerations (Babushkin et al., 1961; Barer, 1962a; Yuganov et al., 1963). V. I. Babushkin et al (1961) relate the increase in tonic stress of the muscles to an increase in static work during accelerations and an intensification of the flux of impulsion from proprioceptors and baroreceptors. There is information to the effect that under the influence of accelerations excitation of many neuromuscular structures and impairment of the peripheral motor coordination occurs resulting in a shift in the function of nerve plexes (Marukhanyan et al., 1962). Thus, the authors attribute the increase in myoelectric activity and impairments of movement coordination to disruptions of the motor system.

In actuality, the appearance of excitation foci in the region of the motor analyzer under the influence of accelerations was noted by B. M. Savin (1957).

D. I. Medvedev (1963), in a microscopic investigation of the brain, after brief accelerations of 8 and 12 g (duration of 3 and 1 min, respectively), discovered a number of morphohistochemical changes in the region of the motor analyzer.

However, there are many data indicating the development of motor disturbances of a typically vestibular character. For example, Winget, Smith and 27 Kelly (1962), during and after prolonged acceleration on a centrifuge 1.5-2.0 g), observed the development of postural and locomotor abnormalities in chicks, accompanied by symptoms of functional disturbances of the labyrinth. Special vestibular tests (rotation around an axis passing through both labyrinths) revealed a change in the duration of postnystagmus and cupulometric parameters. These accelerations caused an increase in sensitivity of the labyrinth of birds.

An increase in the excitability of the vestibular apparatus was also noted by V. A. Shabalin (1961) when human subjects were exposed to an aperiodic angular displacement (accelerations up to 2 g). During rapidly changing accelerations of great intensity there were vestibular disturbances with symptoms of discoordination, involuntary movements of the torso and extremities and trembling (Bruce, Barr, 1963).

Cramer et al. (1963) recorded electronystagmograms of cats during optokinetic irritation after stimulation of the labyrinths (horizontal semicircular canals) by angular accelerations ($0.1-0.4 \text{ rad/sec}^2$). This exposure changed the dynamic characteristic and the amplitude of responses to a series of vestibular stimuli. A change in the character of nystagmic reactions for different values of angular accelerations and "g forces" was also observed by Evans et al. (1962). The authors recorded the motions of the labyrinthine cupula, potentials of the vestibular nerve, nystagmic movements of the eyes, and accelerometer and chronometer data.

An increase in vestibular reactions during a 5 min rotation on a centrifuge was observed in dogs by A. Ye. Kurashvili (1962). An indirect confirmation of the participation of the vestibular apparatus in the reactions of the body to the effect of accelerations may be the discovery by this same author of the disappearance of the autonomous components of the effect (change in pulse and respiration) in animals with surgically removed labyrinths.

These investigations attest to the influence of accelerations either on labyrinth functions in general, or more frequently, on the functions of the semicircular canals. The recording characteristics of reactions and testing samples made possible a study of the cupular component of the vestibular apparatus. We could find no specific investigations of the influence of accelerations on the otolithic component of the labyrinth in the literature available. However, some data indirectly indicate its susceptibility to damage during accelerations. Among such data is the dependence of the nystagmic reaction accompanying human exposure to various magnitudes of angular accelerations on body position relative to the vertical axis of rotation (Markaryan, 1963). The dependence of information from the otoliths on the direction of the resultant radial acceleration was discovered by Schubert and Kolder (1962). 28

The study by Ye. M. Yuganov, I. I. Kas'yan and B. F. Asyamolog (1963) is very interesting. The authors carried out a series of investigations on human subjects and different animals during exposure to accelerations (1-7 g) in parabolic flights aboard aircraft, vertical flights in rockets and during centrifugation. It was found that there is an increase in the tonus and amplitude of bioelectric currents in skeletal muscles (by a factor of 1.5-3.0) during accelerations and a decrease in these same indices during weightlessness. The reaction was manifested particularly clearly in the extensor muscles. Inverse relations were sometimes manifested in extremity flexors (cats and dogs). In animals with surgically removed labyrinths, the bioelectric activity of the muscles remained virtually unchanged. The authors personally interpret the observed effects to be the result of influences from the vestibular analyzer. In addition, if it is taken into account that vestibular-tonic influences on the muscles (especially the extensors) are related to the otolithic component of the vestibular apparatus including utriculi (Magnus, 1924), the participation of the latter in the change of the level of myoelectrical activity during accelerations is entirely possible.

Nevertheless, to investigate the affect of accelerations on the functional state of the otolithic component of the labyrinth, special studies must be conducted using a carefully measured experimental stimulus of this part of the vestibular apparatus.

This study represents an attempt to carry out such an experiment in which the types of vestibular tests and evaluations of response reactions were oriented to study otolithic functions.

The purpose of this experiment was to study the functions of the otolithic component of the vestibular apparatus after the exposure of animals to acceleration. The experimental animals were male guinea pigs, weighing 350-500 g. One group of animals (12 guinea pigs) was subjected to acceleration twice, with a one-day interval, and the second group (16 guinea pigs) served as a control and was not subjected to acceleration. The rotation was conducted at a rate of 135 rpm with an arm radius of 39.5 cm. The duration of each acceleration was 15 min. The 8 g accelerations were in a "back-chest" direction. Experimentation began 7-10 days prior to acceleration, and the animals were then examined 1 (each 10-15 min), 2, 3, 5, 7, 10, 15, 20, 25 and 30 days after acceleration.

A change in the functional state of the vestibular analyzer was monitored as a function of the electromyographic characteristics of the vestibular-tonic reflex in hind leg extensors. The record of the bioelectric activity of these muscles was made during three successive 10-sec periods: before, during and directly after adequate stimulation of the organ of equilibrium. The method for recording myoelectrical activity, adequate measured stimulus of the vestibular apparatus, and procedures for primary and statistical processing of the results have been described in earlier studies (Apanasenko, 1964a). The investigation of functions of the vestibular apparatus was accompanied by examination of the peripheral blood, body weight, and the general condition of the animals. /29

The spontaneous bioelectric activity of the investigated muscles during relative rest (animal seated in a normal pose) immediately after centrifugation increases very sharply (fig. 1). However, this effect does not persist for a relatively long time. Even on the day following the acceleration, the level of background electrical activity of the extensors begins to decrease. In some animals the value of the electrical activity on this day even decreases to normal. By the seventh day after the first exposure to acceleration, the spontaneous muscular activity of all experimental animals was completely normalized and thereafter no longer essentially differed from control activity. The background myoelectric activity in the group of animals subjected to accelerations comes even lower than that of the control group. The curve showing the effect of acceleration is situated along the lower boundary of the control curve beginning on the seventh day. On the 25th and 30th days after acceleration it even exceeds the control level, reflecting an insignificant decrease in the background electrical activity of muscles in experimental animals.

Thus, two different periods in the dynamics of spontaneous electrical activity of the investigated muscles are clearly defined: relatively /30
short--an increase; and more prolonged--normalization of the values along the lower boundary of the control. In the first period, the difference from the control is statistically reliable with respect to both the scatter and the median ($P < 0.001$). In the second period, the indices for animals in the experimental and control groups did not differ reliably with respect to the median ($P > 0.05$).



Figure 1. Change in integral background bioelectric activity of muscles of the hind leg of guinea pigs after acceleration.

x-axis--time after acceleration, in days.
y-axis--value of muscular electrical activity in relative units. 0, mean level of background myoelectric activity before exposure; 1, control; 2, group of animals exposed to acceleration.



Figure 2. Change in total electrical activity of muscles of the hind leg of guinea pigs during adequate stimulation of vestibular apparatus after acceleration. Notations same as in figure 1.

The results were similar for all (except one) of the animals subjected to accelerations. One guinea pig did not show an increase in spontaneous electrical activity of the extensors on the days of acceleration. In this animal during the influence of accelerations, myoelectric activity in a state of relative rest decreased rather strongly, especially on the first seven days after exposure. By the tenth day the changes were small, but a somewhat decreased level of bioelectric activity of the extensors persisted in this animal during the entire investigation. The reaction of the investigated group of muscles to adequate stimulation of the vestibular analyzer was somewhat unique. The bioelectric activity of these muscles during (fig. 2) and directly after (fig. 3) adequate stimulation of the vestibular apparatus by controlled oscillation was essentially the same as the control. Differences from control values were unreliable relative to the median and scatter ($P > 0.05$).

In both cases (during and after reactions to vestibular stimulation), the curves reflecting the effect of acceleration are very similar to one another in shape. Up to the fifth day after exposure they are situated along the lower boundary of the control, and beginning on the seventh day they lie along the upper boundary and a little above it. This absence of changes is apparently related in part to a high level of background electrical activity in muscles on the first day after acceleration. The myoelectric reaction (and its after-effect) to vestibular stimulation does not vary relative to the highly increased electrical activity of the muscles in a resting state. However, in absolute values, excluding the background, on the first three days after acceleration there is a rather significant increase in the electrical activity of the investigated muscles during and directly after adequate stimulation of the vestibular apparatus (figs. 4 and 5). These changes are uniform for all animals of the experimental group.

The latent period of the reaction changes very significantly after exposure to accelerations (fig. 6). Here, as in the case of background electrical activity, there are two clearly expressed phases of change. On the days of acceleration, the latent period of myoelectric reaction to vestibular stimulation decreases very greatly. In some cases we were completely unable to 32 detect the latency of the reaction. On the day after the second acceleration, the decrease in the latent period was no longer as significant; from the fifth

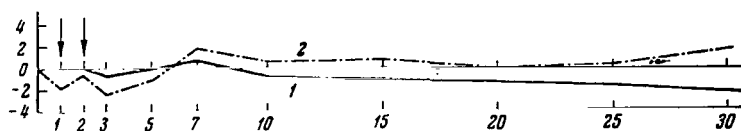


Figure 3. Change in total electrical activity of muscles of the hind leg of guinea pigs during the aftereffect of reaction to adequate vestibular stimulation after acceleration. Notations same as in figure 1.

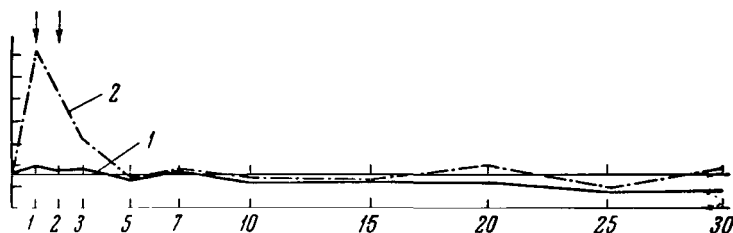


Figure 4. Change in total electrical activity of muscles of the hind leg of guinea pigs during adequate vestibular stimulation after acceleration. Along y-axis--absolute total value of muscular electrical activity disregarding the background electrical activity of these same muscles. Other notations same as in figure 1.

through the tenth day after the first acceleration the latent period is completely normal. However, after the tenth day the latent period of the vestibular-tonic reaction increases considerably and persists at a high level up to the end of the investigation.

Both observed phases of changes (separately) differ reliably from the control with respect to both statistical indices ($P < 0.001$). The scatter within the experimental group in the course of both periods was greater--exceeding by a factor of three the scatter within the control group. The median of changes is first situated 5.2 units below (period I) and then 3.3 units above (period II) the control group. However, the values of the latent period during the entire time after acceleration differ reliably from the control only relative to scatter ($P < 0.001$). The median of the changes, reflecting their opposite direction in the first and second phases, does not change compared to the control

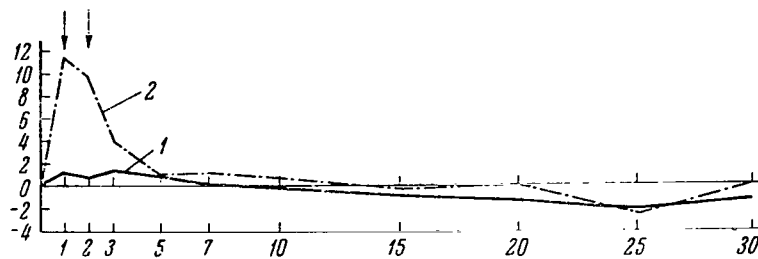


Figure 5. Change in total electrical activity of muscles of the hind leg of guinea pigs during the aftereffect of reaction to adequate vestibular stimulation after acceleration. Along y-axis--absolute total value of muscular electrical activity disregarding the background electrical activity of these same muscles. Other notations same as in figure 1.

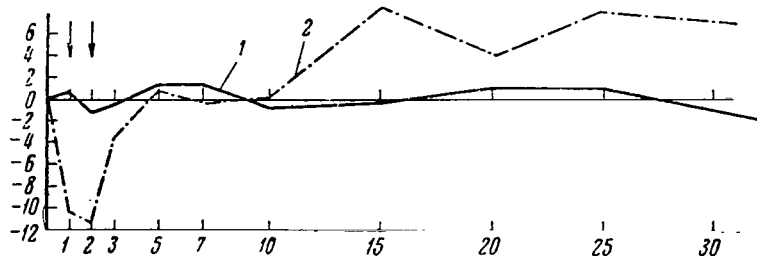


Figure 6. Change in duration of the latent period of reaction to adequate vestibular stimulation after acceleration. Along y-axis--value of latent period in relative units. Remaining notations same as in figure 1.

($P > 0.05$). The changes are completely uniform for all animals of the experimental group.

It is interesting to note the almost directly opposite dynamics of the first phases of the changes in the latent period of the vestibular-tonic reaction and the electrical activity of the muscles in a state of relative rest. However, the phase of increase in the latent period corresponds to a phase of stabilization in background myoelectric activity along the lower

boundary of the control. The directly opposite character of the dynamics is no longer observed here, but there is some correspondence of temporal changes. The duration of the aftereffect of the investigated myoelectric reaction to adequate vestibular stimulation (fig. 7) undergoes wavelike changes after /33 acceleration passing through the zero level. Immediately after acceleration it increases while from the fifth through the tenth days it decreases somewhat and then increases a little, etc. The amplitude of these fluctuations is not very great, but appreciably greater than in the control. The difference from the control is reliable relative to scatter ($P < 0.001$) but unreliable relative to the median ($P > 0.05$).

With respect to this parameter, the changes are uniform for all animals subjected to acceleration. Thus, under the influence of accelerations there is a change in some of the myoelectric characteristics of the vestibular-tonic reflex for the extensors of the hind legs. Prolonged changes occur only in the latent period of the investigated vestibular-tonic reflex. In the remaining cases (spontaneous electrical activity of the muscles, duration of the aftereffect of the reaction to vestibular stimulation), the changes are relatively brief and most clearly expressed on the days of acceleration.

The number of leukocytes in the peripheral blood of the animals increases appreciably after exposure to accelerations (fig. 8). Moderate leukocytosis persists during the entire period of the investigation. Beginning on the 20th day, however, there is a gradual normalization of the number of white /34 blood cells. The difference from the control is statistically reliable ($P < 0.001$).

The effect of accelerations is not reflected appreciably in the general condition of the animals. Directly after centrifugation of experimental guinea pigs, there was decrease in general motor activity, impairment of coordination of movements, and sometimes leaning of the body to one side. After 3-7 min all these phenomena disappeared and the animals did not outwardly reveal deviations from normal. Thereafter, during the entire course of the observations, they differed in no way from control animals. The weight increased (fig. 9) without appreciable differences from the control ($P > 0.05$). Such a trend was observed

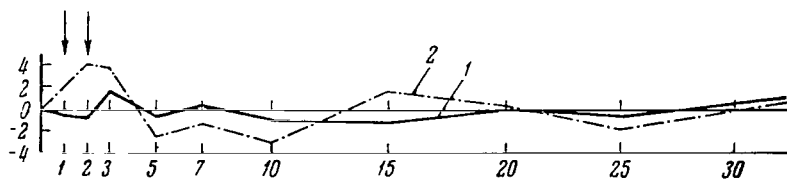


Figure 7. Change in duration of the aftereffect of reaction to adequate vestibular stimulation after acceleration. Along y-axis--duration of aftereffect in relative units. Other notations same as in figure 1.

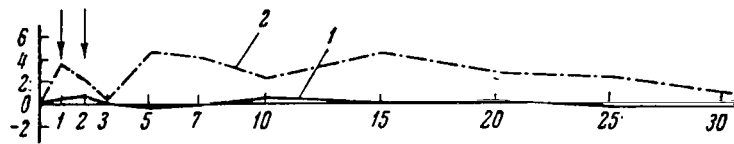


Figure 8. Change in the number of leukocytes in the peripheral blood of animals after acceleration. Along y-axis--number of leukocytes per 1 mm³ of blood in relative units. Other notations same as in figure 1.

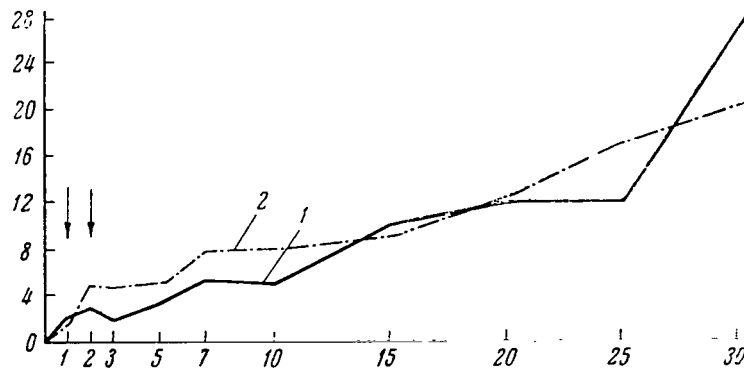


Figure 9. Change in the weight of animals after acceleration. Along y-axis--weight of animals in relative units. Other notations same as in figure 1.

in 11 of the experimental guinea pigs in the postexperimental period. One animal died during acceleration, indicating the substantial magnitude of the acceleration used. It is of interest to compare the effect of acceleration, vibration and space flight conditions on the investigated characteristics of the vestibular-tonic reflex. Figures 10-15 show the simultaneous results of acceleration and two other previously investigated factors (Apanasenko, 1964a).

All three factors cause a strong increase in the spontaneous electrical activity of the extensors during rest (fig. 10). During acceleration the changes are large, but are the briefest. During vibration they are somewhat lesser in magnitude, but very prolonged. The changes occurring after space flight differ with respect to duration and incomparably greater value. It would appear that changes during space flight are the result of the summation of accelerations and vibration. This result apparently is further

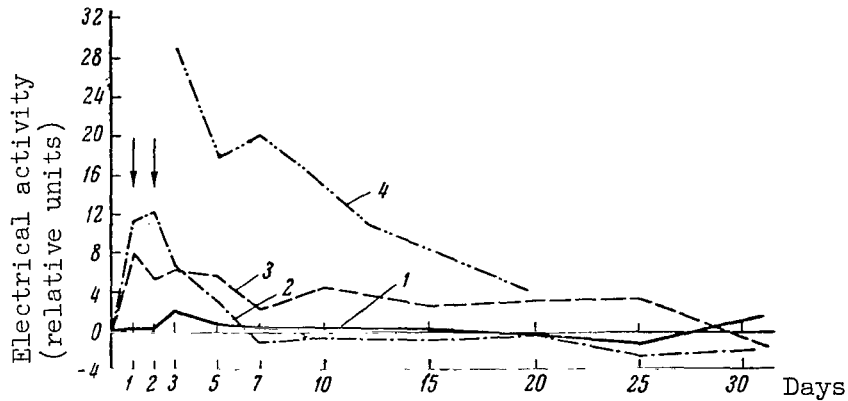


Figure 10. Comparative changes in the total background electrical activity of muscles of the hind leg of guinea pigs after acceleration, vibration and space flight. x-axis--time after acceleration, in days. y-axis--value of muscular electrical activity in relative units. 0, mean level of bioelectric activity of muscles prior to exposure; 1, control; 2, group of animals exposed to acceleration; 3, group of animals exposed to vibration; 4, guinea pig in the flight of the 4th orbital spaceship.

intensified by other space-flight factors. The electromyograms recorded during relative rest (fig. 11) demonstrate a clear gradation of changes: a normal level of spontaneous electrical activity of the muscles before exposure, moderate increase of activity after vibration, a still stronger increase after acceleration and a very strong high-amplitude impulsation after the flight of the fourth orbital spacecraft ("Sputnik-7").

During and in the aftereffect of reaction to adequate vestibular stimulation, the level of muscular electrical activity (relative to the background) varies little after acceleration, decreases somewhat after vibration and has a two-phase characteristic of changes after the flight (figs. 12 and 13). The maximum value of the changes in these cases is observed after the flight. The first phase of the postflight changes (decrease in the bioelectric activity of the investigated muscles) is close in form and value to the effect of vibration. The second phase (increase in myoelectrical activity) can be attributed in part to the effect of accelerations; however, for the most part it apparently reflects the affect of some other flight factors or their combination. However, it is possible that the increase in the background electrical activity of ³⁶the muscles on the first days after the flight was so great that it was at the limit of the myoelectrical capacity. In this case the increase in myoelectric activity during and in the aftereffect of the reaction to vestibular stimulation

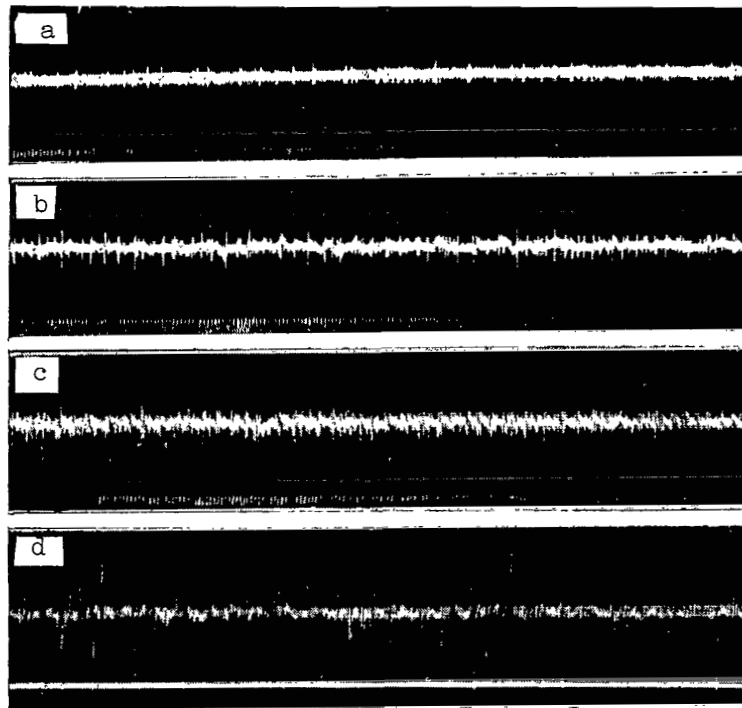


Figure 11. Electromyograms of muscles of the hind leg of a guinea pig in a state of relative rest. a, prior to exposure; b, after vibration; c, after acceleration; d, after the flight of the fourth orbital spacecraft.

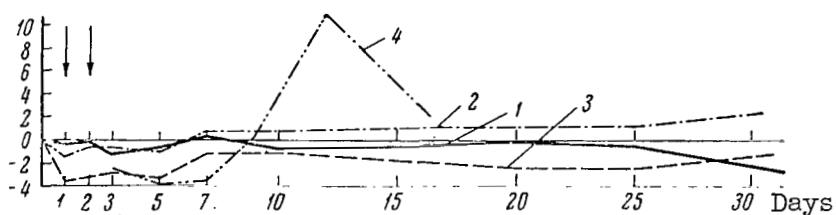


Figure 12. Comparative changes in total electrical activity of muscles of the hind leg of guinea pigs during adequate vestibular stimulation after acceleration, vibration and space flight. Notations same as in figure 10.

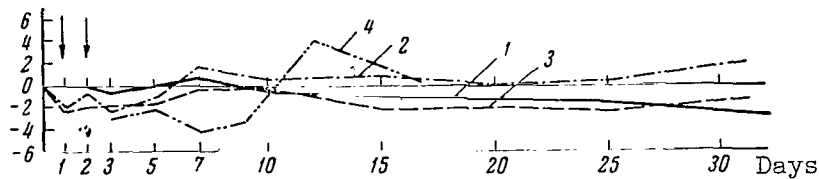


Figure 13. Comparative changes in total electrical activity of muscles of the hind leg of guinea pigs during the aftereffect of reaction to adequate vestibular stimulation after acceleration, vibration and space flight. Notations same as in figure 10.

(relative to the strongly increased background) can be manifested only after a decrease in the level of spontaneous electrical activity to a certain value.

The latent period of myoelectric reaction to adequate vestibular stimulation undergoes two-phase changes after acceleration, decreases considerably after vibration and decreases very greatly after flight (fig. 14). In the latter case the changes are most significant; as far as spontaneous electrical activity of the muscles is concerned, there is a possibility of the partial summation of the effects of vibrations and accelerations in the first period after exposure. Thereafter the effect of acceleration completely differs ^{/38} from the effect of the flight. According to trend and duration of the changes, the effect of space flight is more similar to the effect of vibration than to the effect of acceleration.

Approximately the same relations apply to the duration of the aftereffect of the investigated vestibular-tonic reaction (figs. 15 and 16). After vibration or flight this index increases considerably, and after acceleration it changes in a wavelike fashion passing through the zero level. Relative to magnitude, direction and duration, postflight changes are more similar to changes after vibration. The flight effect is characterized by great instability: the magnitudes of changes first considerably exceed the effect of ^{/39} vibration, then fail to equal it. This phenomenon can be attributed in part to the fact that in this case we are not dealing with mean data from a group, but with individual data from one animal.

Thus, on the basis of all investigated indices, the effect of space flight exceeds the effect of both acceleration and vibration. Sometimes the postflight changes seem to be the result of a summation of the effects of vibration and accelerations.

Relative to the trend and duration of the changes, there is a greater similarity between the effects of space flight and vibration than between the effects of space flight and acceleration.

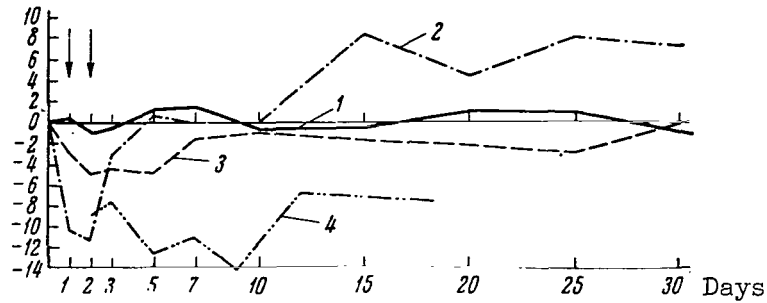


Figure 14. Comparative changes in duration of the latent period of reaction to adequate vestibular stimulation after acceleration, vibration and space flight. y-axis--value of latent period in relative units. Other notations same as in figure 10.

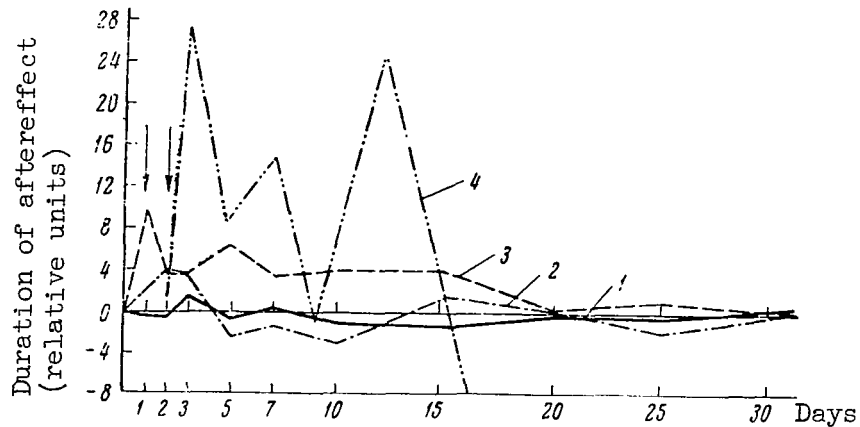


Figure 15. Comparative changes in duration of the aftereffect of reaction to adequate vestibular stimulation after acceleration, vibration and space flight. Along y-axis--duration of aftereffect in relative units. Other notations same as in figure 10.

Conclusion

The increase in spontaneous bioelectric activity of extensors after exposure to accelerations, observed in our experiments fully agrees with data in the



Figure 16. Diagram of values of the duration of the aftereffect of reaction to adequate vestibular stimulation during the entire period after acceleration, vibration and space flight in percent of mean initial level before exposure. 1, Control; 2, vibration; 3, acceleration; 4, space flight. y-axis--duration of the aftereffect of vestibular reaction for the period after exposure, in percent of mean initial level prior to exposure.

literature (Babushkin et al., 1961; Barer, 1962b; Barer et al., 1963; Kotovskaya et al., 1962; Marukhanyan et al., 1962; Yuganov et al., 1963). In contrast to the latter, in this study an investigation was made of a more prolonged aftereffect period. The increase in the level of myoelectric activity, accompanied by an increase in muscle tonus, usually is considered to be a compensatory phenomenon associated with the effect of accelerations (Barer, 1962b; Marukhanyan et al., 1962; Yuganov et al., 1963). The results of this study make it possible to surmise that the increased level of electrical activity of the extensors is caused not only by an intensified flux of afferent impulsion from the proprio- and baroreceptors (Babushkin et al., 1961; Marukhanyan et al., 1962) via the reticular formation in the cerebral cortex (Izosimov and Razumeyev, 1962), but also by vestibular attenuation.

In all probability it is the otoliths which specifically participate in the formation of the myoelectric reaction to accelerations. In particular, it was established long ago (Magnus, 1924) that vestibular influences on the tonus of the extensors is exerted for the most part from the utricle. Since the participation of the vestibular apparatus in the tonic stress of the skeletal muscles during accelerations may be considered as demonstrated (Yuganov et al., 1963), it is the otoliths which should perform this function. An indirect confirmation of this may be the change in electromyographic parameters during specific stimulation of the otolithic part of the vestibular apparatus under the influence of

accelerations, which was noted during our study. Thus, an increase in tonic stress of muscles during accelerations apparently takes place via systems of the motor and vestibular (its otolithic component) analyzers.

The insignificant, but very stable and prolonged decrease of the spontaneous electrical activity of the muscles which we investigated, appearing on the seventh day after exposure, apparently characterizes the period of restoration after strong tonic stress on the days of acceleration. /40

The absence of significant changes in the level of bioelectric activity of the muscles during and in the aftereffect of the reaction to controlled vestibular stimulation can in all probability be attributed to the fact that developing accelerations stimulate the otoliths but are not strictly adequate.

Such accelerations are for the most part transmitted to the semicircular canals where a change in sensitivity during acceleration has been observed by a number of authors (Kurashvili, 1962; Evans et al., 1962; Cramer et al., 1963; Winget et al., 1962; Shabalin, 1961; Bruce, Barr, 1963, and others).

In this connection, for example, vibration, being a stimulus which is more adequate to the otoliths, changes the muscular electrical activity to a greater extent during and in the aftereffect of the reaction to controlled vestibular stimulation than acceleration. Some decrease in the myoelectric reaction to adequate stimulation of the otoliths in the first period (first five days in our experiments) can be attributed to negative induction from systems stimulated to compensate the harmful effect of accelerations (for example, respiration, blood supply, tonus of skeletal muscles). The possibility of such a mechanism is pointed out by M. P. Brestkin (1958) in explaining the inhibition of alimentary reflexes during considerable accelerations.

In addition, we feel that relations may occur here, similar to those observed in human subjects by E. V. Marukhanyan and his associates (1962). During accelerations, there was disruption of the capability for adequate evaluation of a lifted weight; the weight usually was underestimated. The authors feel that against the background of muscle stress which is increased during accelerations, the effort of lifting a weight becomes insignificant. Similarly, additional controlled vestibular stimulation can become less effective, considering the already elevated background electrical activity of the extensors.

This hypothesis appears all the more probable, since, as already mentioned above, the reaction to experimental oscillation is related to the level of myoelectrical activity at rest. In absolute values, disregarding background, on the first days after acceleration this reaction is increased (figs. 4 and 5).

Definite difficulties are involved in an analysis of the considerable changes in the value of the latent period of reaction to adequate vestibular stimulation. The very strong decrease in the latent period on days of acceleration may be evidence of increased excitability of structures of the vestibular analyzer. An increase in mobility of the synaptic formations of the central component of the analyzer is also extremely probable. /41

The literature contains references to the increased excitability of the vestibular analyzer under the influence of angular accelerations (Shabalin, 1961; Winget, Smith, Kelly, 1962). The change in the functional state of the vestibular analyzer is also shown to a certain degree by an increase of tonic stress in skeletal muscles (Yuganov et al., 1963). It is also known that under the influence of accelerations, the functional interrelations of stimulating and inhibiting processes in the cortex and subcortex are disrupted. The predominance of one nerve process or the other is determined by the magnitude and duration of the effect of accelerations and apparently also by a number of other factors (Belay, Vasil'yev, Kolchin, 1964).

Nevertheless, the results of many investigations permit us to assume that in the first period, inhibition processes are disrupted and excitation predominates in the cortex, later replaced by intense inhibition (Barer, Golov et al., 1963; Belay et al., 1964; Izosimov and Razumeyev, 1960; Savin, 1957). Thus, the excitability of the vestibular analyzer in the initial period after acceleration apparently is increased. Ya. A. Vinnikov, O. G. Gazenko et al. (1963) observed in the utricular apparatus of different kinds of animals a combination of histochemical changes indicating the excitation of this organ after exposure to accelerations.

In addition, the almost mirror-like similarity of curves reflecting the change in spontaneous myoelectric activity and the latent period of the reaction to experimental vestibular stimulation suggests that the decrease in the latent period of this reaction may be partly related to the excited state of effector muscles or motor centers. High tonus neuromuscular structures ensure rapid reaction of the effector of the vestibular-tonic reflex; the latent period of response to vestibular stimulation is shortened; however, the degree of this response may remain unchanged. In addition, there probably is also an increase of the functional mobility of the cerebral systems (Barer, Golov et al., 1963). If this hypothesis is correct, the second phase of the change in the latent period of reaction to the testing oscillation could be related to: (a) a restorative stage (four stages, according to Barer, 1962a,b) and (b) the response of the body to external factors. The excitability of the effector neuromuscular structures at this time is greatly decreased and the mobility of the functional systems of the brain is limited. Inhibition processes may predominate in the cortex as a result of overstresses (Barer, Golov et al., 1963; Belay et al., 1964; Izosimov and Razumeyev, 1960; Kislyakov, 1956, 1958). ⁴² The latent period of the investigated vestibular-tonic reaction is considerably increased. The background electrical activity of the extensors is slightly decreased at this time. The long duration of the restoration stage can be attributed to the species makeup of the guinea pigs, whose sensitivity to accelerations is in general characterized by certain peculiarities (Sirotnin, 1961).

The duration of the aftereffect of the investigated vestibular-tonic reaction does not reveal significant changes. A certain increase in this parameter during the first three days apparently reflects a state of increased excitability of the vestibular apparatus and neuromuscular structures.

In our experiments, by the 25th or 30th days after the first acceleration according to a number of indices (myoelectric activity at rest, during and after

vestibular stimulation), there was an insignificant increase in changes compared to the preceding period of almost total normalization. The phenomenon was apparently related to the wavelike character of the course of the restoration period. Similar relations were observed by A. A. Barer (1962a,b). The author notes an intensification of disruptions of conditioned reflex activity in rats from the 22nd-25th up to the 32nd day after exposure. There was a relatively slight resistance on the part of the guinea pigs to the accelerations employed. Eight exposures to acceleration or a rather prolonged acceleration is a highly effective agent. This is also indicated by the death of one animal during acceleration. Nevertheless, the condition of all remaining animals was completely normal during the entire period of the investigation. Some disruption of coordination of movements disappeared completely after 2-5 min.

The changes in electromyographic indices were also relatively small and brief (except for changes in the latent period).

It can be assumed that acceleration causes smaller changes in the functional state of the otolithic apparatus than does vibration, which would appear to be a less harmful agent.

Comparison of the results of a flight experiment and the isolated effects of dynamic factors makes it possible to assert that the effect of space flight on the myoelectric characteristics of the vestibular-tonic reflex is not reproduced by acceleration or vibration. Postflight changes, with respect to all investigated indices, exceed the effects of these factors. In some cases the flight effect is seemingly the result of a summation of the brief effects of acceleration and the effects of vibration (background electrical activity, latent period of the vestibular-tonic reaction), which are somewhat less in magnitude but persistent. Naturally, this notion is very simplified and incomplete. Under flight conditions a major role is played by a whole series of 43 other factors in addition to vibration and accelerations. In addition, it is well known that during the combined effect of a number of factors, each of them may appreciably alter the effectiveness of the other. However, there are some bases for noting that relative to the trend and duration of the effects, the effect of space flight is more similar to the effect of vibration than to the effect of acceleration.

Summary

1. Double exposure of guinea pigs to acceleration ("back-chest" direction, 8 g, 15 min) caused a strong, but relatively brief (day of exposure and the following day) increase in the bioelectric activity of hind leg extensors.
2. The level of electrical activity of the investigated muscles during and in the aftereffect of the reaction to adequate vestibular stimulation (relative to the background electrical activity of the muscles) remains almost unchanged after exposure to accelerations.
3. The latent period of this reaction undergoes considerable two-phase changes under the influence of accelerations. On the days of acceleration the

length of the latent period is decreased sharply, then it gradually returns to normal and after the tenth day, increases appreciably.

4. The duration of the aftereffect of the investigated vestibular-tonic reaction reveals moderate wavelike oscillations at about the zero level after exposure to accelerations.

5. The myoelectric characteristics of the vestibular-tonic reflex change more briefly under the influence of acceleration and in some cases to a lesser degree than after vibration, which for the otolithic apparatus is a more adequate stimulus.

6. The accelerations used have exerted no subsequent significant effect on the general condition and behavior of the surviving (one died) animals. Weight increased normally; the investigation of the peripheral blood revealed insignificant leukocytosis.

7. Comparison of the isolated effects of dynamic factors and space flight conditions shows a greater trend and duration similarity between space flight and vibration than between space flight and acceleration. According to some indices, the flight effects are seemingly the result of a summation of the effects of vibration and acceleration. Neither vibration nor acceleration completely reproduce the effects of space flight.

EFFECT OF MULTIPLE EXPOSURE TO VIBRATION ON THE FUNCTIONAL
STATE OF THE SPINAL REFLEX ARC

M. A. Kuznetsova

ABSTRACT

Guinea pigs were exposed to whole-body vertical vibration 10 times in the course of 16 days (70 cps, 0.4 mm, 15 min). The control animals were placed near an operating vibration stand.

Exposure to vibration caused parabiatic phenomena in the defensive flexor reflex arc.

An inverse correlation was noted between changes in latent period duration and changes in the intensity of threshold electrical stimulus.

In the first part of the period of exposure to vibration there was a cumulation of vibration effects. In the second part of this period reflex activity tended to improve. A succession of parabiatic phases takes place in the reflex arc investigated. This is indicative of a transfer from higher to lower inhibition. This phenomenon is thought to be evidence of incomplete adaptation to vibration.

Vibration stand noise caused changes in the reflexes of the control animals. These changes differed greatly from those in the experimental animals.

The ever-increasing use in modern technology of equipment with a large 45 number of revolutions and impacts and with a high frequency of oscillations, as well as the vigorous development of aviation and cosmonautics, makes it fully understandable why researchers are showing such interest in the multiple effects of vibration. Numerous clinical investigations have shown that prolonged contact with a source of vibration leads to the development of serious illness, in which all organs and systems suffer without exception. Considering the present status of investigations of the pathology of vibration sickness, it becomes obvious that injury to the nervous system is not only its only leading symptom, but also the principal cause of total illness.

The school of Ye. Ts. Andreyeva-Galanina, whose studies for the most part have been concerned with the pathogenesis of this illness, advances the

hypothesis that the development of vibration sickness is caused by the development of a parabiogenic condition in nervous system centers, especially in the spinal cord. The basis for such an assumption are investigations which indicate that during low intensity vibrations or in the case of a sufficiently strong nervous system, relatively resistant to such vibrations, an excitatory process of certain intensity will develop in different parts of the nervous system. This was discovered during investigations of the neuromuscular apparatus and the motor analyzer (Shcherbak, 1903a, b; Saltykovskiy, 1927; Goldmann, 1948; Terent'yev, 1958; Donskaya and Stoma, 1960; Drogichina et al., 1961), of the vestibular analyzer (Borshchevskiy et al., 1958b; Usenko, 1961; Apanasenko, 1964a), of the autonomic nervous system (Borshchevskiy et al., 1963) and also in conditioned reflex and encephalographic investigations (Butkovskaya, 1951; Butkovskaya, Koryukayev, 1963).

With an intensification of vibration stimulus or with an increase in 46 its duration, there is an increase of the stimulation process along with the formation of centers of stagnation (Mel'kumova, 1960; Rumyantsev, 1961; Artamonova, 1964), and transition to a state of inhibition (Mogendovich, 1961; Tartakovskaya, 1964). In such cases it is often possible to observe phase phenomena. With respect to the cerebral cortex they are considered to be the result of the development of protective inhibition (Butkovskaya, 1957a, b; Zuyev, 1960; Butkovskaya, Koryukayev, 1963; Karchmazh, 1962). For the lower parts of the central nervous system the phase state is considered by most investigators to be the result of development of parabiosis (Sazon-Yaroshevich, 1956; Pavlova, 1958; Kovalevich, 1960; Mel'kumova, 1960; Drogichina, 1961; Abramovich-Polyakov, 1962; Madorskiy, 1963; Stoma, 1963, 1964).

These phenomena are observed in many parts of the CNS, but are manifested with particular clarity in investigations of the neuromuscular and motor analyzers. The possibility of adaptation to such a harmful agent is of definite interest, especially since there are indications in the literature that even brief exposure to whole-body vibration with relatively low parameters is capable of inducing considerable and prolonged impairments of the CNS (Apanasenko, 1964a; Kuznetsova, 1964a). The problem arises as to the optimal conditions for adaptation, its possibilities and limits and the mechanisms which govern it.

Until now only a limited number of investigations have been devoted to this problem. There are studies indicating a decrease of unpleasant sensations and autonomic disruptions during prolonged or repeated exposures to vibration

(Cörmann, 1940; Kulikovskiy, 1939; Croce¹, 1948; Butkovskaya, 1959). The greatest number of studies indicating adaptation to repeated exposure to vibration are devoted to higher nervous activity and the bioelectric activity of the brain (Mikheyeva, 1955; Skachedub, 1957; Butkovskaya, 1951; Gurovskiy, 1959; Terent'yev, 1958; Karchmazh, 1962; Artamonova, 1963). It follows from these studies that for adaptation to occur, the vibration stimulus should cause

¹Published in I. Ya. Borshchevskiy et al., 1963.

changes of definite intensity in the CNS, that is, it should not be very weak (Gurovskiy, 1959), but neither should it be exceptionally strong (Butkovskaya, 1951; Borshchevskiy, Koreshkov et al., 1958b; Gorbachevskiy, 1959). The possibility of adaptation is also determined by the initial functional state and type of nervous system (Andreyeva-Galanina and Lebedeva, 1951; Mekheyeva, 1955; Skachdub, 1957). The occurrence of adaptation frequently is preceded by a cumulation of disruptions caused by initial exposures to vibration (Gurovskiy, 1959). Other studies have been made in which attenuation of the effect /47 was not observed with repeated exposure.

There have been very few studies devoted to an investigation of the motor analyzer and neuromuscular apparatus in which the adaptation phenomenon is observed. Most authors, using a multiple vibration stimulus, say nothing at all about the dynamics of disruptions and discuss only the final results. Some investigators state that there is no adaptation in the absence of supporting experimental data (Minetskiy, 1960; Stoma, 1964).

The purpose of our study was to trace the dynamics of changes in the functional state of the defensive motor reflex arc during multiple exposure to whole-body vertical vibration.

Method

The experiment was conducted on 14 male guinea pigs, weighing 350-500 g, divided into two groups. One group of animals was subjected to vibration ten times; this was done in five series with two vibrations per series. The interval between each exposure was one day. The intervals between pairs of exposures to vibration were two-three days. Vibration was vertical with a frequency of 70 cps, amplitude of 0.4 mm and a duration of 15 min. Another group of animals served as control and was exposed to noise from an operating vibration stand (about 75 dB).

As indices of the functional state of the investigated reflex arc we selected the threshold of stimulation and the latent period of the unconditioned defensive motor reaction. The recording of the latent period was accomplished with an accuracy up to 0.5 m/sec, using a method already described (Kuznetsova, 1964a). An alternating current from a sonic generator with a frequency of 70 cps with three gradations was used as a pain stimulus. In order to exclude the influence of abrupt changes of the thresholds on the value of the reflex responses, we used stimuli of constant physiological intensity.

1. Weak stimulus, always equal to three times the threshold value.
2. Intermediate stimulus, always equal to the threshold value multiplied by 6.
3. Strong stimulus, always equal to the threshold value multiplied by 10.

In all cases the duration of the stimulating impulse was 0.03 sec.

/48

The following procedures were followed in the experiment.

1. Determination of the threshold.
2. Determination of the latent period of the reflex to a weak stimulus (three measurements).
3. Checking the threshold value.
4. Determination of the latent period of the reflex to a stimulus of intermediate intensity (three measurements).
5. Checking the threshold value.
6. Determination of the latent period of the reflex to a strong stimulus (two measurements).

After the normal limits of fluctuations of the investigated parameters (4-5 experiments) were established (two weeks), the animals were exposed to vibration.

For convenience, we will henceforth use the term "vibration period" for the period during which the animals were exposed to vibration. Investigations of the animals were made on the 2nd, 4th, 6th, 8th, 9th, and 10th days of exposure to vibration.

The period of observations after termination of exposure to vibration will henceforth be called the postvibration period. Observations were made on the 1st, 3rd, 5th, 8th, 10th, 13th and 18th days. An investigation of these parameters was accompanied by examinations of the peripheral blood, weight and physiological condition of the animals.

For comparison of the results obtained for groups of animals with a different initial level and variability of the investigated parameters, each absolute value measured after exposure was expressed in percentage deviation from the mean initial value of this parameter. The computed percentage deviations were divided by the mean group scatter of these values prior to exposure. The results were subjected to statistical processing using the median and

χ^2 tests.

Experimental Results

Figure 1,A,1 shows data obtained for a control group of animals subjected to the noise of an operating vibration stand. Analysis of the results reveals

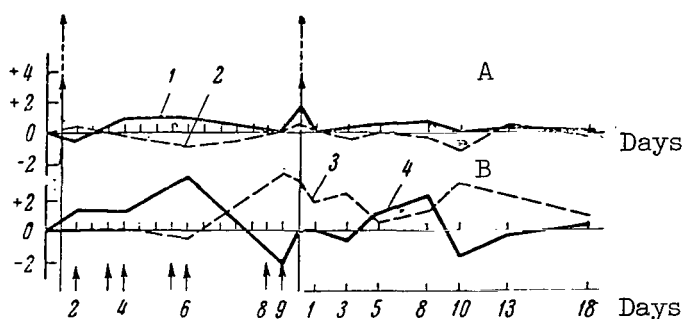


Figure 1. Change in the intensity of threshold stimulus in experimental and control groups. A, Mean value of threshold stimulus intensity; 1, in animals of control group; 2, in animals multiply exposed to vibration; B, individual changes in the threshold stimulus intensity in animals of control group; 4, in guinea pig No. 96; 3, in guinea pig No. 83. x-axis--time in days; y-axis--intensity of threshold stimulus, expressed in percent of deviation from mean initial value, divided by mean group scatter prior to exposure. Arrows indicate days of exposure. Large arrows indicate the beginning and end of the vibration period.

that in most of the animals the value of excitability thresholds (stimulation) fluctuated during the entire period within the limits of initial scatter. Only two animals showed an appreciable increase in the intensity of threshold stimulus. In guinea pig No. 96 such a phenomenon was observed twice: on the day of the 6th exposure to noise and on the 8th day of the postexperimental period (fig. 1,B,4). In guinea pig No. 83 the intensity of threshold stimulation increased on the day of the 9th exposure, and was maintained at this 50 higher level up to the 13th day of the postexperimental period (fig. 1,B,3).

Definite changes were observed in the values of the latent period in the control group. The animals can be divided into two groups on the basis of the character of the changes in reflex responses. In one group (fig. 2,A) there was a tendency towards an increase in latent periods of the investigated reactions; in the other there was a tendency towards shortening of the latent periods (fig. 2,B). These changes were manifested for the most part in the vibration period. The changes were cumulative, attaining maximum value by the 4th day of exposure to the noise stimulus. In most of the animals the investigated values already began to return to the initial level in the experimental period. In animals of the first group, fluctuations of the values of the latent periods in the postvibration period did not exceed the limits of normal average group scatter. In animals of the second group on the 3rd-5th day of the postvibration period there was a second decrease in the investigated values.

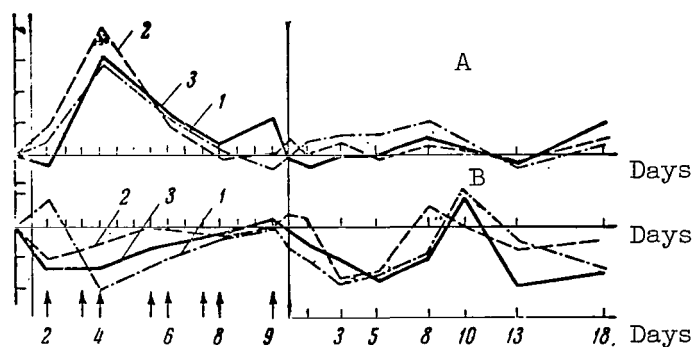


Figure 2. Change in value of the latent period of the unconditioned defensive motor reaction in animals of the control group. A and B, mean value of latent period in two groups of control animals; 1, weak; 2, intermediate; 3, strong, physiologically constant stimuli. y-axis--latent period, expressed in percentage deviation from mean initial value, divided by mean group scatter prior to exposure (1 graduation = 1). Vertical lines--beginning and end of vibration period. Other notations same as in figure 1.

The changes of the characteristics of the reflex reactions in the group of control animals were such that in most cases correct intensity relations were maintained between responses to stimuli of different intensity, with the exception of the 4th day of exposure to sound stimulation, when in the first group there were stronger changes in the reactions to a stimulus of intermediate intensity. A count of the experiments with a disruption of intensity relations revealed very insignificant deviations from the initial background (fig. 5, III). Thus, exposure to noise was not indifferent to the reflex activity of the investigated animals. Despite the fact that in some animals it caused an increase in reflex conductivity and in others a decrease, the general group medians in the reactions to all three types of stimulus were lower ($Me_3 = -0.5$, $Me_6 = -0.1$, $Me_{10} = -0.4$), which is an indication that in the control group of animals there

was a predominant tendency toward decreasing values of the investigated parameter. Since considerable disruptions of reflex activity were observed in only half the animals (and even those were brief), on the basis of this material no reliable difference ($P > 0.05$) from the initial background was discovered in the control group of animals.

In contrast to the control group, in animals multiply exposed to vibration there were considerable changes in the values of the latent period of the investigated reactions. In some of the animals these changes could be traced

during the entire period of the observations. The animals were divided into three groups on the basis of types of reaction to vibration.

In the animals of the first group (Nos. 89, 100, 103, fig. 3), there was a considerable increase in the latent period of reactions to intermediate and strong stimuli, whereas the latent period of reactions to a weak stimulus either remained unchanged or changed very insignificantly (in No. 103, ^{/51} tended to increase and in No. 100, tended to shorten). In most cases reactions to a strong stimulus suffered to a greater extent, and only in guinea pig No. 100 were there more severe disruptions of reactions to a stimulus of intermediate intensity in the course of the first five days of the postvibration period.

Thus, in the change of the functional state of the investigated reflex arc in this group of animals there was a disruption of correct force relationships relative to the types of adjustment and paradoxical phases at a low level. It should be noted that such a disruption did not occur immediately. Guinea pig No. 100 in the first one and one half weeks of the vibration period showed a decrease in the value of the latent period of reactions to a weak stimulus, whereas reactions to intermediate and strong stimuli remained within the limits

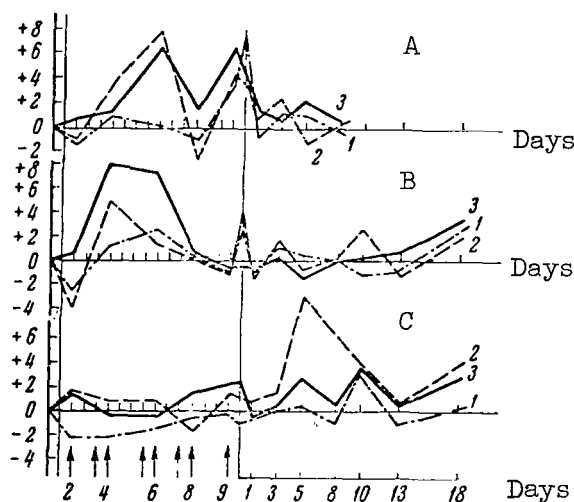


Figure 3. Change in value of the latent period of the unconditioned defensive motor reaction during multiple exposure to vibration in animals of the first group.

A, B and C, individual changes in the latent period for guinea pigs Nos. 89, 103 and 100, respectively. Other notations same as in figure 2.

of the mean group scatter. Therefore, at this stage the proper force relationships was disrupted with respect to the type of adjustment phase at a high level (fig. 3,B). Such an increase in reflex activity was also observed in guinea pigs Nos. 89 and 103 on the day of the 2nd exposure to vibration /52 (fig. 3,A,B). The functional disruptions of the investigated reflex arc, occurring under the influence of vibration, gradually increased and attained their maximum value in guinea pig No. 100 by the 5th and 10th days of the post-vibration period, while in guinea pigs Nos. 103 and 89, by the 4th and 6th days of exposure to vibration. The paradoxical phase observed on these days was later replaced by a low level adjustment phase. In guinea pig No. 89 on the day of the 8th vibration there also was an intermediate stimulus phase.

In two animals of this group (guinea pigs Nos. 89 and 103) there was rather rapid onset of a period of normalization of reflex activity. The normalization of correct force relationships took place via a narcotic phase. In guinea pig No. 89 on the day of the next-to-last vibration the latent period of the reaction to a weak stimulus, which until then had varied within the range of the initial level, not exceeding the limits of mean group deviation, increased sharply. Its changes on the day of the last vibration were even more significant than the changes of the latent period for intermediate and strong stimuli. On the day following the termination of exposure to vibration there was a sharp decrease in the values of the investigated parameters, although they still somewhat exceeded the normal mean group scatter.

In guinea pig No. 103, for which the values of the latent periods of the reactions to all three types of stimulus already began to return to the initial level with the 8th exposure to vibration, on the day of the last vibration a narcotic phase was noted in the functional state of the reflex arc, as in guinea pig No. 89. At the same time that the reaction to a strong stimulus remained within the limits of fluctuations of the initial background, there was a repeated increase in latent periods of reactions to weak and intermediate stimuli. Thereafter, in the course of the entire period of observations, the investigated parameters fluctuated insignificantly. Only on the 18th day of the postvibration period was there again an increase in the latent periods of all three reactions, although not as strong as during the vibration period.

In the third animal belonging to this particular group (guinea pig No. 100) there was no tendency towards normalization of reflex activity. The values of the latent period of the reactions to intermediate and strong stimuli were maintained at a high level during the entire period of observations. On the first five days after termination of exposure to vibration, there were stronger disruptions of reactions to an intermediate stimulus.

These disruptions of reflex activity are also clearly manifested in experiments where disruptions of proper force relationships occurred. Figure 5,1 shows that in the vibration period there was a sharp increase in the percentage of correct force relationships between reactions to weak and strong, weak /53 and intermediate, and intermediate and strong stimuli. Therefore, during this period, disruption of adjustment and paradoxical phases predominated.

In the postvibration period, the number of experiments with disruptions of force relationships decreased appreciably. The relationship between reactions to weak and strong, and also to strong and intermediate stimuli was within the range of the initial level (fig. 5, I, A, B, 3). An increase in the number of experiments with adjustment of reactions to intermediate and weak stimuli (fig. 5, I, B, 3) for the most part is caused by changes in reactions to an intermediate stimulus in guinea pig No. 100.

In the second group of animals (guinea pigs Nos. 99 and 101) changes in the investigated parameter were far less significant than in the group considered above, but as in guinea pig No. 100, they were traced during the entire period of investigation. In this group of animals (fig. 4) during the vibration period the latent periods of reactions to weak and strong stimuli increased at the same time that the latent period for a stimulus of intermediate intensity was even shortened relative to the initial level. Such a change in force relationships with respect to the type of intermediate stimulus phase was maintained in guinea pig No. 101 up to the 9th day of the exposure to vibration, while in guinea pig No. 99 up to the 5th day of the postvibration period. A considerable time after exposure, the change in reflex activity of guinea pig No. 99 took place; here, proper force relationships with respect to the type of narcotic phase were preserved. The increase in the latent period compared to the initial background was identical in the reactions to all ¹⁵⁴ three types of stimulation. In guinea pig No. 101 on the day of the last vibration the status of the intermediate stimulus phase was replaced by a paradoxical phase at a low level. The latent periods for the intermediate and strong stimuli were higher, whereas reactions to a weak stimulus returned to the initial state. The dynamics of changes in the investigated parameter during the postvibration period is evidence of the difficulty of reflex normalization. Days in which relative restoration took place were replaced by periods

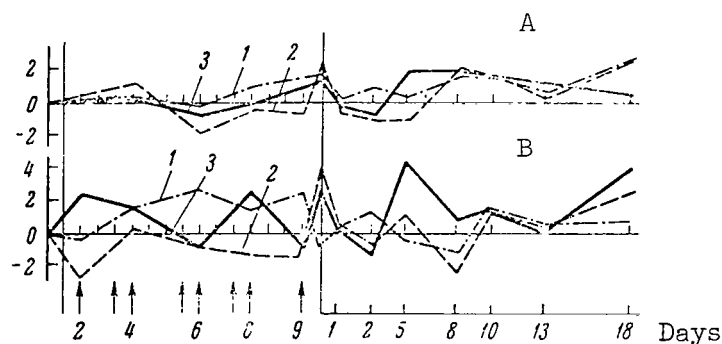


Figure 4. Change in value of the latent period of the unconditioned defensive motor reaction during multiple exposure to vibration in the second group. A and B, individual latent period changes in guinea pigs Nos. 99 and 101, respectively. Other notations same as in figure 2.

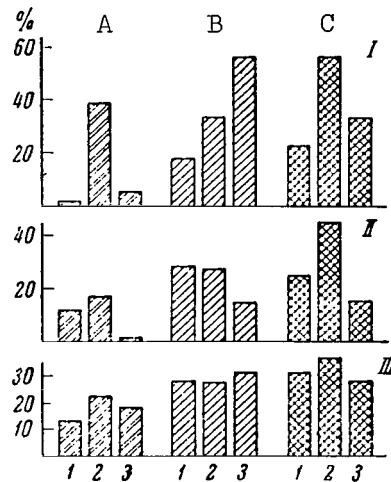


Figure 5. Disruptions of force relationships. I, First group of vibrated animals; II, second group of vibrated animals; III, control group. Disruptions of force relationships in reactions: A, to weak and strong; B, to weak and intermediate; C, to strong and intermediate stimuli. 1, Prior to exposure; 2, during vibration; 3, postvibration. y-axis--number of experiments (in percent) with disruptions of force relationships.

of disruption, in which there were adjustment and paradoxical phases at a low level (the 5th and 18th days after exposure to vibration).

All these data are confirmed in experiments with disruptions of the proper force relationships. Figure 5 shows that in the vibration period there was a sharp increase in the percentage of experiments with disruptions of proper force relationships between reactions to intermediate and strong stimuli (II,B), whereas between reactions to weak and strong and weak and intermediate stimuli, changes in force relationships varied within the same limits as the control group (II,A and B). Therefore, in this period there was a predominance of disruptions of the proper force relationships relative to the type of intermediate stimulus phase.

After termination of vibration, the number of experiments with these disruptions decreased, even when compared to the initial background (fig. 5,II,3). This indicates that in the postvibration period, the change in the functional

state of the investigated reflex arc was for the most part, reflected by all of the characteristics of a narcotic phase. Thus, both individual curves and total experiments with disruptions of proper force relationships are evidence that the primary disruptions in the investigated reflex arc in these groups of animals occurred during exposure to vibration and were reflected by a tendency towards disruption of correct force relationships, relative to both the type of adjustment and paradoxical phases at a low level or to the type of intermediate stimulus phase. This tendency was quite clearly expressed, because it appeared in both the relative and absolute values of the investigated parameter. /55

A very unique reaction was observed in guinea pig No. 81 (third group). As can be seen from figure 6, in the period of exposure to vibration there were sharp disruptions of reflex activity in reactions to all three stimuli. On the day of the second exposure to vibration, the investigated values still changed very insignificantly. Thereafter these disruptions cumulated and attained their maximum value by the 4th-6th day of exposure to vibration.

Despite the fact that the increase in the latent period of all reactions was approximately identical, as a result of which proper force relationships were maintained, the disruption of reflex activity in this animal must be regarded as the most severe. In the investigated arc, there was such a strong decrease in reflex conductivity that the transmission of nerve impulses was depressed for all types of stimuli.

A similar reaction was observed in the animals of the first group subjected to the effect of noise from the operating vibration stand (fig. 2,A). However, at this time, as in the control group, the values of the investigated parameters began to return to the initial level beginning with the 6th exposure to the noise stimulus; in guinea pig No. 81 the transmission of nerve impulses remained depressed during the entire course of the vibration period. In addition, the functional state of this arc on the day of the next-to-last vibration period exhibited a low level paradoxical phase inasmuch as the latent period of reflexes to a weak stimulus began to shorten while values of the latent period for a high intensity stimulus remained prolonged. During the postvibration period,

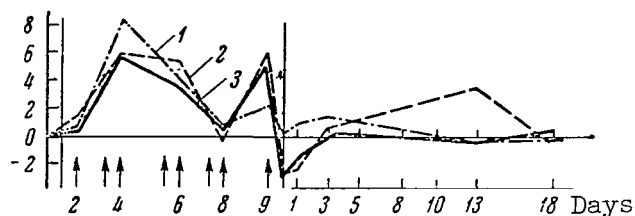


Figure 6. Changes in value of the latent period of the unconditioned defensive motor reaction during multiple exposure to vibration in animals of the third group (guinea pig No. 81). Notations same as in figure 2.

the investigated parameters returned rather rapidly to the initial level; on the first days there was an abbreviation of latent periods of reflexes to intermediate and strong stimuli.

An analysis of changes in the latent period of the investigated reactions shows that the effect of multiple exposure to vibration without exception caused a depression of unconditioned reflex activity. In contrast to the control group, the medians of the averaged combinations of the latent periods of reactions to all three types of stimulus were high. However, the intensity of depression and the character of its manifestation differed. Reactions to stimuli of intermediate ($Me = +1$) and high intensity ($Me = +0.6$) underwent the 56 greatest changes. With respect to this index, the differences from the control group in the reactions to both stimuli were statistically reliable ($P < 0.01$). Since in most of the experimental animals the change in reflex activity corresponded to disruption of force relationships, a reliable difference from the control was not observed ($P > 0.05$) in the change of the latent period of reactions to a weak stimulus ($Me = +0.11$).

With respect to the value of the thresholds of stimulation (excitation), we did not observe such uniform changes in experimental groups as were noted in animals twice exposed to vibration (Kuznetsova, 1964a). In some animals there was a decrease in the intensity of threshold stimulation (fig. 7,A), in others an increase (fig. 7,B), and in still others a change in the value of the

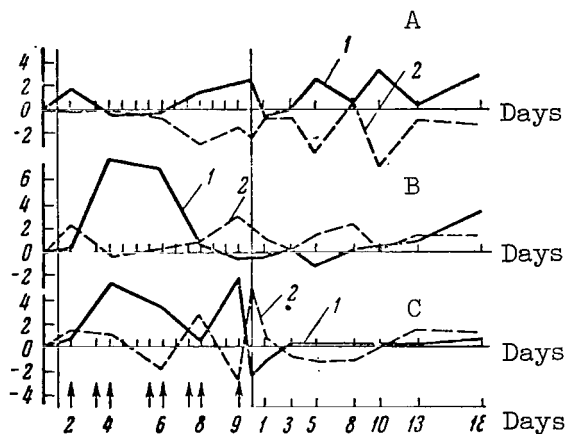


Figure 7. Interrelationship of changes in the value of threshold stimulus with changes in the value of the latent period of the unconditioned defensive motor reaction to a strong stimulus in the group of animals multiply exposed to vibration. Individual changes in the intensity of threshold stimulus (2) and values of latent period (1) in guinea pigs No. 100 (A), 103 (B) and 81 (C). y-axis--investigated parameters in relative units. Other notations same as in figure 2.

threshold stimulus with a peak-like character. The investigated value first increased, then dropped below the initial level (fig. 7,C). As a rule, these deviations were not significant and statistical processing did not reveal a reliable difference between the fluctuations of this parameter in animals of the experimental and control groups (fig. 1,A). However, with respect to the character of the changes in these indices in both groups, there were interesting differences. Figure 7 shows that in the animals repeatedly exposed to vibration there was a clearly expressed inverse correlation between changes in the intensity of threshold stimulation and the value of the latent period of reactions to a strong stimulus. Table 1 shows the distribution of all observed types of the relationships of changes in latent periods of reactions to a strong stimulus and stimulus thresholds in the experimental and control animals.

The table shows both the percentage of animals in which this phenomenon was observed and the percentage of experiments in which it was observed. Note that in control group, one parameter remained within normal limits, whereas the other increased or decreased (type II). Such a form of reaction occurred in 45.4 percent of the cases and in most of the animals (62-75 percent). The different types of reactions were encountered in approximately an identical

TABLE 1. CORRELATION OF THRESHOLD STIMULUS INTENSITY AND LATENT PERIOD VALUES IN EXPERIMENTAL AND CONTROL ANIMALS

Group	I Both parameters normal		II One parameter normal, the other changes								III Parallel change of both parameters				IV Parameters change in a different manner			
	L	T	L	T	L	T	L	T	L	T	L	T	L	T	L	T	L	T
	N	N	>	N	<	N	N	>	N	<	>	>	<	<	>	<	<	>
Control animals,% cases,% total % of cases		100 34.4	75 10		62 14.4		75 12		75 9		50 4.3		22 4		22 3.3		22 7.7	
Experi- mental animals,% cases,% total % of cases		83 34	83 19		16.6 1.1		33 4.7		16.6 3.5		50 4.7		- -		83 17.8		33 3.5	
		34.4			45.4						8.3				11			

NOTES: L, latent period; T, threshold; N, investigated parameter within normal limits; >, investigated parameter increases; <, investigated parameter decreases; I-IV, forms of reaction.

number of cases (9-14 percent). Those forms of reaction in which both parameters changed in the same manner (type III) or their dissociation was observed (type IV) were noted far more rarely (8-11 percent) and in a lesser number of animals (22-50 percent). In the group of animals exposed to vibration there was a decrease in the number of type II reactions. While in the control group this form was encountered in 45.4 percent of the cases, here it was discovered in only 33 percent. The highest percentage was for that type of reaction in which the value of the threshold stimulus remained within the limits of the initial level and the latent period increased. This type of reaction was encountered in 19 percent of the cases and in most of the animals (83 percent), whereas the remaining types of reactions were observed very rarely (1.1-4.7 percent) and in a small number of animals (16.6-33 percent).

The number of cases of type III of reactions in which the changes in both parameters were almost parallel was reduced by almost half. The decrease ^{/58} in the first two types of reactions in the animals of the experimental group was due to an increase in the number of type IV reactions in which there was a dissociation in the change of the investigated parameters. While in the control group this form was encountered in only half of the animals (11 percent of the cases), in the group multiply exposed to vibration it was observed in the majority (83 percent) of the animals (21.3 percent of the cases).

Thus, analysis of the table reveals that multiple exposure to vibration caused a definite disruption in the relationships between values of the latent period and the intensity of threshold stimulus and increased by a factor of two the number of cases of reactions in which both investigated indices changed in a different manner.

Multiple exposure to vibration caused reliable changes in the peripheral blood of the animals ($P < 0.001$). Figure 8 shows that, beginning with the 9th exposure to vibration, the number of leukocytes per 1 mm^3 of the blood of the experimental animals increased. Moderate leukocytosis was observed during the entire period of observations. With respect to change of weight, no reliable differences from the control were observed ($P > 0.05$). However, the group of

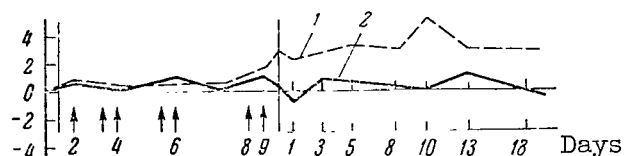


Figure 8. Change in the number of leukocytes in the peripheral blood of animals under the influence of multiple exposure to vibration. 1, Experimental group; 2, control. y-axis--number of leukocytes per 1 mm^3 of blood in relative units. Other notations same as in figure 2.

animals exposed to vibration was characteristically more excitable. During the experiment the animals were restless in the chamber: they jumped, gnawed the walls of the chamber, uttered murmuring sounds and made attempts to escape. It was necessary to wait until they were calm, and sometimes the experiment had to be postponed.

Conclusion

As demonstrated in our earlier investigations (Kuznetsova, 1964a), double exposure to vibration with these same parameters induced in the functional state of the investigated arc of unconditioned defense motor reaction clearly observable changes characterized by the occurrence of parabiogenic states. In some of the animals there was an increase of reflex conductivity with a disruption of force relationships with respect to the types of high-level adjustment phase. In the remaining group of animals the disruptions of force relationships were like an adjustment phase at a moderate level or an intermediate stimulus phase and indicated a more intense state of overexcitation of the motor centers.

This dissimilarity of responses apparently was governed by the characteristics of the nervous system and its initial state. In animals with insufficiently strong inhibition and stimulation processes the state of overexcitation under the influence of vibration could set in very rapidly, which was immediately reflected by complicated transmission of nerve impulses. At the same time, in animals having quite strong stimulation processes the state of overexcitation did not develop, although the observed increase in the conductivity of nerve centers was not complete.

Similar results were obtained by L. D. Luk'yanova in a study of the ¹⁶⁰ change of oxidation processes in the tissues of the motor centers of the cortex and subcortex in white rats exposed to vibrations of similar intensity (Luk'yanova, 1964b). In most of the animals, during the first five minutes of exposure to vibration the author discovered a state of excitation of the nerve cells, which later underwent transition into a state of intense inhibition. In some of the animals the state of excitation in a somewhat less clearly expressed form was also maintained after exposure to vibration. The author believes that these animals had a strong nervous system. Even three-day exposure to vibration stimulus could not induce overexcitation of their nerve centers. This group of animals, with respect to reaction, resembles the first group of animals considered in our investigations. Finally, in the third group of animals the development of intense inhibition was observed from the first minutes of vibration. This group resembles our other two groups and apparently may be classed as animals of the weak type.

The lucid study of M. F. Stoma (1964) is interesting. The author investigated the state of the Achilles reflex during application of a proprioceptive stimulation of different intensities (in supine, sitting and standing positions). Daily three-hour vibration of the rear paw of rabbits (frequency 30 cps, amplitude 1.5 mm) for a period of 1-3 months caused a stable state of excitation

which appeared to be dominant in the corresponding motor centers of the spinal cord. In some of the animals this dominant center had a pathological character. In the reactions to stimulation of different intensities it was found that there are disruptions of the proper force relationships for the types of adjustment and paradoxical phases.

In this investigation, as in the experiments of L. D. Luk'yanova, in some of the animals a gradual transition from a state of excitation to a state of parabiogenic inhibition was observed. An increase in reflex conductivity of the investigated arc in guinea pigs Nos. 89 and 103 on the day of the second exposure to vibration and in guinea pig No. 100 in the course of the first one and one-half weeks of the vibration period, as in animals of the first group twice exposed to vibration, was accompanied by disruption of proper force relationships for the type of adjustment phase at a high level (fig. 3). In another group of animals, although there was no similar increase of the reflex activity of the investigated arc, rapid development of the state of inhibition was not observed.

By the second exposure to vibration in this group of the animals, the investigated parameters were still within the limits of initial fluctuations. With repeated exposures to vibration the resulting effects were cumulated, and in all animals without exception there were various degrees of overexcitation. A tendency was noted towards disruptions of the proper force relationships for types of the intermediate stimulus phase and the adjustment and paradoxical ⁶¹ phases at a low level; there also was a state of intense inhibition of unconditioned reflex activity with retention of the proper force relationships, which in Pavlov circles is called the narcotic phase.

There is no established opinion in present-day physiology as to what position this state occupies among the hypnotic phases. From our point of view, for the solution of this problem it is important to take into account the level at which reflex activity occurs. For example, in guinea pig No. 81 in the first half of the vibration period proper force relationships were maintained between reactions to stimuli of different intensity. In the motor centers of the investigated reflex arc a state of overexcitation developed which was similar to a state of inhibition. The transmission of nerve impulses was greatly hindered in the reactions to all three types of stimulation. This was a narcotic phase at an extremely low level of reflex activity, close to a state of inhibition (fig. 6). We have a different situation in an analysis of the data obtained for guinea pigs Nos. 89 and 103 (fig. 3,A,B). The narcotic phase observed in these animals on the day of the last vibration is an indication of weaker disruptions than those which occurred on the preceding experimental days. Although the latent period of the reactions to a weak stimulus increased in both animals, the transmission of nerve impulses from a strong stimulus returned to the initial level in guinea pig No. 103, whereas in guinea pig No. 89 it tended to accelerate. This was the narcotic phase, but at a relatively higher level of reflex activity than on the preceding experimental days.

Beginning with the second half of the vibration period, despite the fact that the vibration stimulus continued to operate, in some animals there was a

tendency towards relative normalization. In the functional state of the motor centers there was a successive replacement of the parabiogenic phases, evidence of a transition from more intense to less intense inhibition. For example, in guinea pig No. 89 (fig. 3,A) there was successive replacement of the paradoxical phase at a low level (6th exposure to vibration), the intermediate stimulus phase (8th exposure to vibration), and adjustment phase at a low level (9th exposure to vibration). In guinea pig No. 103 (fig. 3,B) the paradoxical phase at a low level (4th exposure to vibration) was replaced by an adjustment phase at a low level (6th exposure to vibration) and a narcotic phase (10th exposure to vibration). In guinea pig No. 81 (fig. 6) the narcotic phase at an extremely low level of reflex activity (4th and 6th exposures to vibration), evidence of a sharp inhibition of reactions to all three types of stimulus, was ¹⁶² replaced on the day of the 9th vibration by a paradoxical phase at a low level, and then by a state of increased conductivity of nerve impulses in reactions to intermediate and strong stimuli (the 10th vibration and the 1st day of the postvibration period). The latter circumstance apparently is evidence of an increase in the lability of the nerve centers, because on this day this animal showed a considerable increase in excitability thresholds of the investigated reflex arc (fig. 7,C,2).

In those animals in which impairments of reflex activity were traced during the entire period of observations, the changes of reflex activity in the aftereffect were insignificant and for the most part were of the narcotic phase type, which was also evidence of a tendency towards partial restoration of the initial functional state of the investigated nerve arc.

Thus, a tendency towards relative and difficult restoration of reflex activity during repeated exposure to vibration appears in our investigation with a definite clarity, and from our point of view can be attributed to a transition of the nerve cells of the motor centers to a new functional level, that is, an adaptation phenomenon. In our opinion, this is supported by successive replacement of parabiogenic states with transition of the motor centers from a state of intense overexcitation to the initial level and even to a level of higher lability.

We believe it improbable that the vibration which we used could cause any irreversible organic changes in the nervous system which would require intervention of compensatory mechanisms. Structural disruptions of the nerve cells of the spinal cord in most cases are discovered during exposure to vibration of great intensities, applied over a considerable interval of time (Shcherbak, 1907a,b; Loecle, 1950; Novotny and Uber, 1959; Minetskiy, 1960; Karpova, 1963a,b). Other confirmations of this idea are the data of L. D. Luk'yanova, A. V. Kol'tsova, Ye. S. Meyzerov and Ye. P. Kazanskaya, obtained in the course of multiple exposure of white rats to vibration with similar parameters (p. 99).

It must be emphasized that we observed the most clearly expressed normalization of reflex activity only in those animals in which exposure to vibration caused a strong response reaction (guinea pigs Nos. 81, 89 and 103). A higher reactance of the nervous system apparently facilitates a more rapid

appearance of adaptation mechanisms. Perhaps these data also confirm the hypothesis that a definite level of changes must be induced for the appearance of adaptation in the nervous system. A similar conclusion was drawn by /63 N. N. Gurovskiy in an investigation of the conditioned reflex activity of white rats, subjected to repeated vibration with a frequency of 45 cps and an amplitude of 0.3 mm. The adaptation to 30-min vibration arising on the 4th-7th day of exposure also persisted when there was an increase of the time of its application to 1-1.5 hr. However, the adaptation developing after repeated 10-min vibrations was disrupted even with an increase in the duration of vibration to 30 min (Gurovskiy, 1959).

The effect of local repeated vibrations on the functional state of the unconditioned defense flexor reflex was studied in a rabbit by N. I. Karpova (Galat). After exposing the rear paw of the animal to vibration of different intensities and studying the intensity and the time of the reflex development of muscular stress, the author concluded that repeated exposure not only does not decrease the effect, but even intensifies it. This conclusion apparently has only limited significance. It follows from the data reported by the author (Galat, 1960, Karpova, 1963a,b): (a) the maximum cumulation of the effect occurs precisely in the period, when in our investigations as well, disruptions were maximum; unfortunately, the author discontinued exposures at this point; (b) the effect of repeated vibration in the experiments of Karpova (Galat) also depended on magnitudes of the initial changes. The initial exposure to 5-min vibration with a frequency of 20 cps did not cause any change in the value of the latent period of the investigated reaction, which remained within the limits of the initial fluctuations. The second vibration increased the reflex time by 0.12 sec. At the same time, 10-min vibration with a frequency of 50 cps (the amplitude in all cases was 2 mm) after the first exposure caused an increase in the latent period by 0.1 sec in comparison with the initial level. On the other hand, the second vibration no longer produced a further increase of the reflex time. It only somewhat increased the interval during which the latent period of the investigated reflex was maintained at such a high level.

Data indicating the presence of a quite clearly expressed inverse correlation between the changes in the latent period value of reactions to a strong stimulus and the intensity of threshold stimulation are of definite interest in our investigation, although on the basis of these data they were not statistically reliable (table 1). It is assumed that the intensity of threshold stimulation is the most important determinant of the excitability of the reflex arc, whereas the value of the latent period (particularly reactions to a strong stimulus) to a greater degree characterizes its functional lability.

Among animals subjected to vibration 10 times there was a predominance of a change in the functional state of the investigated reflex arc, in which /64 reflex excitability increased (the intensity of the threshold stimulus decreased) and physiological lability decreased (the latent period of the reactions to a strong stimulus increased).

There are references in the literature indicating that the appearance of a definite dissociation between changes of excitability and lability in the nervous

system is one of the manifestations of a parabiogenic state. In particular, the state of the nervous system in which there are changes of excitability and lability, similar to those described, is adjusted by the second phase of parabiogenesis (Golikov, 1957; Andreyeva-Galanina, Butkovskaya, 1960).

In any case, the difference in the trend of changes in the values of both parameters, which we observed, was noted for the most part in the vibration period, that is, at the time when parabiogenic phase phenomena were most clearly expressed in the condition of the motor centers.

Comparative analysis of the effect of twofold and tenfold vibration reveals that repeated exposure to a vibration stimulus can cause stronger disruptions of unconditioned reflex activity, apparently due to the cumulation of their harmful effects. In the group of animals subjected to multiple vibration, there was not a single animal in which there was a shortening of the latent periods of the reactions to all three types of stimuli. Twofold vibration in some of the animals caused a similar increase in unconditioned reflex activity, which was traced during the course of the entire period of the investigation (Kuznetsova, 1964a). At the same time, among the animals subjected to tenfold exposure to vibration, there was a development of paradoxical phases at a low level in the motor center and a state of extreme inhibition (narcotic phase at an extremely low level), which was never observed among animals twice exposed to vibration.

However, the fact that in animals twice exposed to vibration changes in the functional state of the investigated reflex arc in most cases corresponded to the third phase (decrease in reflex excitability and physiological lability), while in the case of tenfold vibrations--only to the second phase of parabiogenesis (according to N. V. Golikov) apparently was associated with a relatively more clearly expressed normalization of reflex activity in the latter case.

In a study by Z. M. Gvozdikova it is postulated that the change of transmission of nerve impulses in the arc of the defensive flexor reflex is determined primarily by disruptions in the intercalary neuron, as the youngest phylogenetically and therefore a particularly brittle link (Gvozdikova, 1965). The latent period of unconditioned reflex motor reactions apparently is determined by the state of synaptic transmission of nervous excitation, since the synapse is the least labile formation. N. Ye. Vvedenskiy believes that the synapse is responsible for the development of a state of "pessimism" in the neuromuscular apparatus. Such a hypothesis has been proposed by A. V. Lebedinskiy and Z. N. Nakhil'nitskaya, who assume that the disruption of reflex activity should be attributed primarily to a change in synaptic formations of the central part of the reflex arc (Lebedinskiy and Nakhil'nitskaya, 1960).

As demonstrated by our investigation, the effect of the noise of the vibration stand (75 db) was not indifferent to the reflex activity of the investigated animals. In some animals there was an increase in the conductivity of the nerve impulses in all reactions, which indicates an increase in the lability of the nerve centers of the investigated reflex. In other animals there was a considerable decrease in reflex activity. On the day of the 4th exposure

to noise there was an inhibition of the transmission of nerve impulses in the reactions to all three types of stimulus.

There are indications in the literature that noise of adequate intensity and duration causes a state of overexcitation and inhibition in centers of the cerebral cortex and spinal cord (Khaymovich, 1960; Panayoti, 1963;

Artamonova¹, 1964). However, in our investigations such changes, observed in some of the animals, were brief. In most cases the investigated parameters returned to the initial level at the same time a cumulation of effects from repeated exposure to vibration in the experimental group occurred. Similar results were obtained by N. N. Livshits and Ye. S. Meyzerov in an investigation of the conditioned reflex activity of white rats multiply exposed to a noise stimulus of similar intensity (p. 61).

We believe that such a reaction of the motor centers to the effect of a noise stimulus should be regarded as the result of attenuation (stimulation or inhibition) from the auditory analyzer.

Summary

1. Guinea pigs were exposed ten times to vertical vibration (70 cps, 0.4 mm, 15 min). Significant, statistically reliable changes in the conditions of the motor defensive reflex arc were observed which persisted for 34 days.

2. These changes were characterized by complex changes in the value of the latent period of the investigated unconditioned reflex reaction and the appearance of an inverse correlation between changes in this parameter and the intensity of the threshold stimulus.

3. The dynamics of changes in the latent period of reactions to stimuli of various intensities is evidence of the development of parabiogenic states of different intensities and depths in the investigated reflex arc.

4. This change in the functional state of motor centers predominates when reflex excitability increases and physiological lability decreases (second phase of parabiosis, according to N. V. Golikov).

5. In the first half of the period of vibration exposure there is a cumulation of vibration effects. Beginning with the second half, there is a tendency towards relative restoration of reflex activity. In the function of the investigated spinal arc, there is a successive replacement of parabiogenic phases, indicating a transition from a more intense to a less intense state of inhibition. We believe that this phenomenon can be attributed to a transition of

¹Cited in the article: Ye. Ts. Andreyeva-Galanina, Some Unsolved Problems in the Study of Vibration (O Nekotorykh nereshennykh voprosakh v uchenii o vibratsii), Gigiyena truda i profzabolevaniy, No. 8, 37, 1964.

motor centers to a new functional level, e.g., adaptation. The observed adaptation was incomplete and quite complicated.

6. The completeness of adaptation and the rapidity of its appearance depend on the magnitude of initial changes.

7. Vibration stand noise caused definite changes in the investigated reflex arc which were not statistically reliable.

EFFECT OF VERTICAL VIBRATION AND NOISE ON THE CONDITIONED REFLEXES OF RATS

N. N. Livshits and Ye. S. Meyzerov

ABSTRACT

Rats were exposed three times to whole-body vertical vibration (70 cps, 0.4 mm, 15 min). The interval between the first and second exposures was 14 days, and between the second and third exposures was 7 days. The control animals were placed near the operating vibration stand at the time the experimental rats were subjected to vibration. The motor alimentary reflexes of the rats were investigated.

In rats with a high initial level of conditioned reflexes vibration caused inhibition, with disruption of the relationship between the level of the conditioned reflexes and the stimulating factor. There were significant individual differences in the responses of higher nervous activity to vibration. In some animals the conditioned reflexes disappeared entirely under the influence of vibration, whereas in others they only decreased.

In rats with low initial level of conditioned reflexes vibration caused an increase in the conditioned reflexes, disinhibition of differentiation, and phase phenomena.

In the control animals subjected to vibration stand noise the changes in conditioned reflexes were considerably less clearly expressed than in the experimental animals.

It has been demonstrated in numerous investigations by clinicians, /68
hygienists and physiologists that exposure to vibration causes considerable changes of the functions, and when the exposure is for a long period, it is also accompanied by disruptions of different parts of the CNS. Much experimental data have been generalized in special summaries (Andreyeva-Galanina, 1956; Andreyeva-Galanina et al., 1961; Borshchevskiy et al., 1963; Luk'yanova, 1964a).

The effect of vibration on higher nervous activity was studied by investigating the effect of this factor on human performance of some tasks and by the conditioned reflex method. In subjects during vibration, there was slowing down of writing a standard text, appearance of errors in oral counting and decrease in accuracy performing motor acts (Terent'yev, 1959; Catterson et al., 1962; Borshchevskiy et al., 1963; Barvitenko, 1964, and others).

Vibration effects also cause changes in conditioned reflex activity.

Z. M. Butkovskaya (1952, 1957b) observed an inhibition or distortion of the conditioned reflexes in human subjects after exposure to local vibration of the distal phalanx of the index finger. The parameters of vibration were: frequency 50 and 100 cps, threshold intensity or 3-24 dB above threshold, duration 15 min.

V. G. Terent'yev (1958, 1959, and I. Ya. Borshchevskiy et al., 1963) investigated the effect of whole-body vertical vibration (10-70 cps, 0.4-2.4 mm, duration 4 hr) on the conditioned and unconditioned vascular reflexes of man. A single 4-hr exposure with an amplitude of 0.4 mm for all these frequencies exerted no significant influence on the investigated indices. After repeated exposure or after exposure to greater amplitudes there were changes in the conditioned reflexes, both in the direction of increase and decrease. In 169 some cases differentiations were disinhibited.

The effect of whole-body vibration with a 45 cps frequency, amplitude of 0.3 mm and a duration of 1.5 hr in human subjects caused a lengthening of the latent periods of the motor reaction of choice (Gurovskiy, 1959).

Lengthening of the latent periods of the conditioned reflex with oral reinforcement was found in nail factory workers, subjected to the occupational effects of vibration. The degree of lengthening of the latent period was related with length of time on the job (Zuyev, 1960, 1962).

V. A. Shabalin (1962), using human subjects, observed a stabilization of the latent periods of conditioned motor reflexes at a mean level with oral reinforcement after vibration with a frequency of 15-18/min and an acceleration of 1.5-2 g.

V. V. Andrianov (1958, 1960) discovered considerable discrepancies of higher nervous activity among patients with a cerebral form of vibration sickness. On the basis of investigations by the associative experiment method (used by A. G. Ivanov-Smolyanskiy) and clinical observations, the author concluded that in these patients there was decrease in the intensity of the inhibition process, increase in the inertia of the stimulation process and impairments of interaction between the signal systems.

The effect of local vibration with a frequency of 100 cps on different parts of the canine body at a small amplitude (precise parameters were not indicated) induced in dogs an increase in the motor defense conditioned reflexes and disinhibition of differentiations. After vibration of high amplitude there was extinction of the conditioned reflexes (Mikheyeva, 1955; Skachedub, 1957).

S. A. Karchmazh (1956, 1962) describes the effect of whole-body vertical vibration with a frequency of 20 and 50 cps and amplitudes of 0.40-1.50 mm on the motor alimentary reflexes of laboratory rats. Two-hour vibration caused a lengthening of the latent periods and sometimes also an extinction of the

conditioned reflexes. The effect was proportional to the amplitude of vibration and did not depend on frequency.

N. N. Gurovskiy (1959) used the same method in an investigation of the effect exerted on rats by whole-body vertical vibration with a frequency of 45 cps, amplitude of 0.3 mm and duration of 30-40 min. Among the animals there were cases of extinction of conditioned reflexes and disinhibition of differentiations.

In dogs, vibration caused a decrease in motor and secretory defense reflexes.

Thus, according to the data in the literature, vibration most frequently induces decrease or distortion of positive conditioned reflexes, but cases of their increase are also described. The latent periods become longer, but sometimes are stabilized at a mean level. Some authors observed disinhibition /70 of differentiations. These investigations were made by different methods using whole-body and local vibration.

The purpose of our study was to obtain additional quantitative data on the problem of the effect of whole-body vertical vibration on higher nervous activity.

Data and Method

We worked with rats, using the L. I. Kotlyarevskiy conditioned motor alimentary reflex method. The recording system devised by M. B. Gol'dberg et al. (1962) was used, somewhat modified by V. P. Kornil'yev.

A seven-member stereotype was developed among the rats. Positive stimuli were used: a tone with a frequency of 1000 cps (tone+) and light--lamp with an intensity of about 2 W in the chamber, each three times in the experiment, and differentiation--a tone with a frequency of 400 cps (tone-), once during the experiment.

The integral intensity of the conditioned reflex was determined in relative units, using the product of the amplitudes of the movements of the small door blocking access to the food tray, and the duration of the conditioned motor reaction.

This value was determined from the integrator indicators.

Food was taken away from the animals four hours prior to the experiment. The investigations of the effect of vibration and noise began after firm establishment and stabilization of the stereotype, carrying out food deprivation tests, and the extinction and restoration of the conditioned reflex to tone.

These tests were deemed inadequate for obtaining complete information on the type of higher nervous activity, but the initial conditioned reflex background and some individual characteristics of the animal could be studied during the preliminary analysis, which required 5-8 months.

The experiments were conducted on male rats, sexually mature by the onset of the processing. Six of these rats were exposed to vibration, and ten served as a control. Prior to the onset of vibration, three experimental rats (1, 2 and 20) were used as controls. The experimental group included four "Wistar" and two "August" rats; the control group consisted of six "Wistar" and four "August" rats. One of the experimental rats ("Wistar" No. 4) differed considerably from the others with respect to its characteristics of higher nervous activity, and the experimental results for this rat therefore were not included in the general statistical processing of the data from the principal experimental group; they are presented separately. Each of the individual experimental rats had two partners in the control group with approximately similar indices of higher nervous activity. The results of the experiments on 71 five experimental and ten control rats were processed statistically, using the median and Student tests.

The experimental rats were exposed to whole-body vertical vibration three times; the vibration had a frequency of 70 cps, amplitude of 0.4 mm and duration of 15 min. The vibration was accompanied by noise with an intensity of about 75 db. During this same time, the control rats were in individual boxes near the operating vibration stand. The first and second vibration periods were separated by two weeks, and the second and third vibrations were separated by one week.

Experimental Results

The very first experiments revealed that the noise of the vibration stand induced definite changes in the conditioned reflexes of the rats. Prior to the onset of vibration, three experimental rats (Nos. 1, 2 and 20) were exposed three times to the influence of the noise of the vibration stand, but it was not possible to fully extinguish the reaction to this stimulus in these rats.

As was determined from further experiments, this required a large number of repetitions. The elimination of the effect of the noise component, therefore, was accomplished by comparison of the reactions of the experimental and control rats.

In five rats which we assigned to the main experimental group, the reaction to exposure to vibration was uniform, with sharp quantitative individual differences.

The conditioned reflexes decreased in all five rats, but the degree of decrease was not identically expressed.

Prior to exposure, "August" rats Nos. 20 and 22 were characterized by a high level of conditioned reflexes, with considerable variations in their magnitude from experiment to experiment and frequent cases of extinction. The force relationships were correct in the overwhelming majority of experiments, differentiations were expressed well, but were unstable. During the experiment the rats were extremely mobile, frequently turning away from the food tray.

Deprivation of food caused a disruption of differentiations. In this case in rat No. 20 the conditioned reflexes increased, but in rat No. 22 the conditioned reflexes on the first days of stimulation were absent in this experiment.

After the first exposure to vibration, the conditioned reflexes in these rats disappeared completely on the days of vibration (the experiment was conducted immediately after vibration). On the following days the conditioned reflexes in rat No. 22 were manifested in some of the positive stimuli, remaining low. The values of the conditioned reflexes changed in a wavelike fashion. The experiments in which conditioned reflexes were absent were replaced by experiments with decreased condition reflexes; restoration of the initial level of conditioned reflex activity did not occur during the two weeks after the first vibration period. /72

A similar picture was observed on the first days after vibration in rat No. 20, but conditioned reflexes were absent only on the day of exposure; beginning with the eighth day after vibration, there began a restoration of the initial level of the conditioned reflex activity. Rats Nos. 1 and 2 of the "Wistar" line prior to exposure were characterized by high conditioned reflexes, always with correct force relationships, stably persisting at a constant level for a number of months, and absolute differentiations.

After exposure to vibration, there was an indistinct decrease in the positive conditioned reflexes in both rats, in contrast to rats Nos. 20 and 22, not reaching zero. On the following days the values of the conditioned reflexes decreased and increased in wavelike fashion. A full restoration to the initial level was observed on the sixth-seventh day.

In rat No. 18 ("Wistar" line) the conditioned reflexes were very high, 2-3 times higher than in all other rats of the particular breed used both in this and in other parallel studies. The values of the reflexes varied at a high level; differentiation was relative. The ratio of the intensity of the reaction to differentiation to the intensity of the reaction to the positive

stimulus paired with it, (index $\frac{\text{tone-}}{\text{tone+}}$), averaged 38 percent. Normally, there

were phase phenomena at low and high levels and an incomplete ultraparadoxical phase. We were not able to select any completely corresponding partners in the control group for this rat, but since it was the most resistant to the effect of vibration, we included the data obtained for it in the statistical processing. They could only decrease, and in no case increase the difference between the experimental and control. After the first exposure to vibration, the

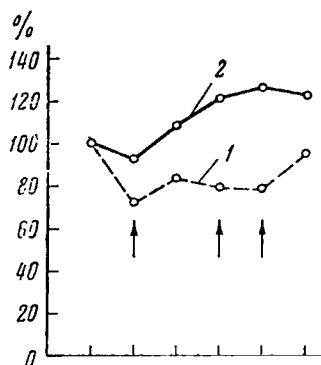


Figure 1. Effect of vibration and noise on mean total value of conditioned reflexes to positive stimuli (rats of main group). Along x-axis --time after exposure, in weeks. Along y-axis--mean total value of intensity of conditioned reflexes in experiment, expressed in percent of initial background, assigned value of 100 percent. Mean intensity of reflex prior to exposure was computed with data from 20-30 experiments on each rat of particular group; after exposure--based on data from 6 experiments. 1, Rats exposed to combined vibration and noise; 2, rats exposed to noise of vibration stand; arrows indicate times of exposure.

decrease of the values of the conditioned reflexes in this rat was the most clearly expressed and was observed only directly after exposure.

The reaction to subsequent exposures changed differently in various rats. There was a gradual increase in the reaction with an increase in the number of vibrations (rat No. 18). At the same time we recorded gradual attenuation of the reactions (rat No. 20), and a weaker reaction to the second exposure and a considerably enhanced reaction to the third exposure (rats Nos. 1 and 2) and inverse relations (rat No. 20).

Figure 1 shows the changes of the mean total intensity of the conditioned reflexes in the control and experimental groups.

The differences between the experiment and control with respect to this index were reliable according to the median test ($P < 0.01$). It is impossible to judge the changes of the reaction to repeated exposures on the basis of averaged data due to the nonuniformity of these phenomena in different animals. /73

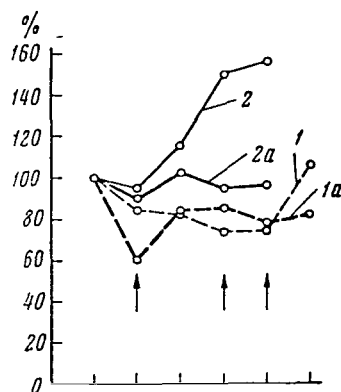


Figure 2. Effect of vibration and noise on mean intensity of positive conditioned reflexes to 1000 cps tone (tone+) and light (rats of main group). Along y-axis--mean intensity of conditioned reflex, expressed in percent of initial background, assigned value 100 percent. 1a, 2a, Tone+, 1, 2, light. Remaining notations same as in figure 1.

Adaptation or compensation leading to weak reactions to multiple exposures appeared in our experiments after a large number of exposures, and attrition of these mechanisms and intensification of the vibration effect appeared considerably later (see articles by L. D. Luk'yanova et al., and M. A. Kuznetsova, this volume). Therefore we could not detect these phenomena in our experiments, but it was, nevertheless, possible to check the reproducibility of the vibration effects.

The decrease in conditioned reflexes, both with respect to mean total intensity and separately for strong and weak stimuli, remained stable during the entire period of the exposure (figs. 1 and 2).

The influence of the vibration stand noise on conditioned reflex activity differed appreciably from the effect of vibration. The mean total intensity of the conditioned reflex differed only after the first exposure to noise; after the second it returned to the initial level; after the third it considerably exceeded the initial level. The difference between the experimental and control groups with respect to this index was reliable according to the median ($P < 0.01$). /74

The decrease in the reflex to a strong stimulus at all stages of the investigation was sharper in the experimental group (fig. 2); the differences were statistically reliable according to the median ($P < 0.05$). The most clearly expressed decrease in this index after the first exposure was not observed in all animals and was not reliable. The conditioned reflex to light decreased in the control group only after the first exposure to noise, and

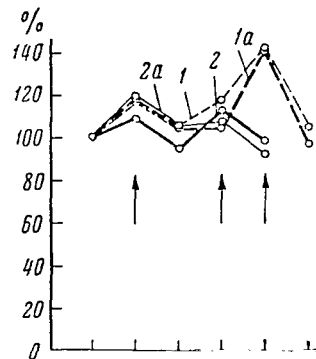


Figure 3. Effect of vibration and noise on mean latent periods of the conditioned reflexes (rats of main group). Along y-axis -- mean values of latent periods, expressed in percent of initial background, assigned value 100 percent. 1a, 2a, Tone 1000 cps; 1, 2, light. Remaining notations same as in fig. 1.

after further exposures it increased. The differences between the experimental and control groups were so obvious, that there was no need of statistical checking of reliability (fig. 2).

The latent periods of positive conditioned reflexes to both stimuli lengthened under the influence of vibration; the most significant lengthening was after the third exposure (fig. 3). By this time there was a clear difference between the experimental and control groups. In the latter there was also lengthening of the latent period of the conditioned reflexes, however, by the third exposure this reaction was completely extinguished, whereas in the experimental group the changes were maximal under similar conditions.

The latent period of the conditioned reflex reflects not only the intensity of the stimulation process, but mobility as well. Ye. Ts. Andreyeva-Galanina and Z. M. Butkovskaya (1960) discovered in certain workers subjected to industrial vibration a decrease in excitability and increased lability of the muscles of the thenar group, which is one of the initial phases of development of the paralytic process. We therefore checked the correspondence of the dynamics of the changes of the latent period of the conditioned reflexes and changes of the intensity of this index. Dissociation phenomena (shortening of the latent period with decrease of the intensity of the conditioned reflex) were discovered in two experimental rats, but similar phenomena were equally common in the control group. It is possible that the negative result can be attributed to the fact that the increase of mobility in our experiments was masked by a considerable decrease of excitability.

The number of cases of disruption of correct force relationships after exposure to vibration increased reliably ($P < 0.05$, fig. 4). As mentioned above,

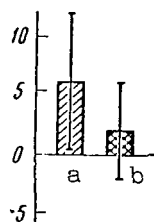


Figure 4. Influence of vibration and noise on number of phase phenomena (rats of main group). Along y-axis--change of number of phase phenomena in comparison with initial background. Phase phenomena expressed in percent of number of conditioned reflexes present. a, Rats subjected to combined vibration and noise; b, rats subjected to noise of vibration stand. Lines on bars represent mean error, multiplied by t corresponding to $P < 0.05$.

under the influence of vibrations there was an increase in the number of extinctions of conditioned reflexes, and experiments occurred in which conditioned reflexes were absent. Therefore, for comparison with the initial level, we determined the ratio of the number of phase phenomena to the number of conditioned reflexes present, not the mean number of phase phenomena in the experiment.

In the overwhelming majority of cases in the animals of this group there were adjustment, paradoxical and ultraparadoxical phases present at a low level. In rats for which these phenomena were also normally characteristic, their number increased. After exposure to vibration, phase phenomena at a low level were also noted in those animals for which they were never normally observed (rats Nos. 1 and 2).

In rat No. 18, after the third vibration exposure, a complete ultraparadoxical phase was recorded, which had never been observed earlier.

In the control group the number of phase phenomena increased, but this increase was less significant than in the experimental group.

In contrast to the experimental rats, in the control animals the increase in the number of phase phenomena in comparison with the initial background was not statistically reliable, despite the fact that the number of animals in this group was twice as great, which increased the possibility of detection of the reliability of the changes.

In those rats in which the decrease in conditioned reflexes caused by vibration was not very sharp, the differentiations were disinhibited (rats Nos. 1, 2 and 18). In these same cases, when vibration caused a considerable

depression of the conditioned reflexes, the reactions to differentiation weakened. This was expressed not only in a decrease of the absolute values of the reactions, but also in a decrease of the index $\frac{\text{tone-}}{\text{tone+}}$ (rats Nos. 20 and 22).

In the control group the disinhibition of differentiations was observed in two rats; no dependence was discovered between the disinhibition of differentiations and change in the intensity of the positive conditioned reflex. The differences between experimental and control with respect to this index /76 cannot be considered reliable on the basis of our material.

In one rat (No. 4) there were sharp differences from the remaining experimental animals already apparent during preliminary processing. The conditioned reflexes for this rat were very low in intensity: 84 percent of them were absent. Often it took food only after additional stimulus (a knock on the food tray), and sometimes took no food at all. Daylong deprivation of food still further weakened the artificial and natural conditioned reflexes, on the basis of which we concluded that its excitation processes were extremely weak.

In this rat the noise of the vibration stand caused a decrease in positive conditioned reflexes; after the first exposure there was also disinhibition of differentiations, which indicated a weakness of the inhibition process as well. After triple exposure to noise, conditioned reflexes and reactions to differentiation fell to zero and remained at this level for two weeks. The first exposure to vibration was carried out against this background. The intensity of the conditioned reflexes immediately increased, exceeding the initial level, but the latent periods decreased (figs. 5 and 6). During the second week after exposure the conditioned reflexes increased sharply. After the second and third exposures the conditioned reflexes began to decrease, but remained above the initial level. Simultaneously with an increase in conditioned reflexes, there was a decrease in the number of rejections of food. During the last week prior to the onset of exposure to vibration there were 21 rejections of food, and after the second exposure only four. At the same time, the conditioned reflex background remained unstable, and increases in conditioned reflexes alternated with their decrease to zero. By this time differentiation was disinhibited (fig. 7), but the index $\frac{\text{tone-}}{\text{tone+}}$ decreased.

The increase in positive conditioned reflexes was accompanied by an /77 increase in the number of phase phenomena to the number of conditioned reflexes present, from 6 to 31 percent. An adjustment phase at a high level after the first vibration exposure was apparent, even on the basis of averaged data for the indices of the intensity of the conditioned reflex (fig. 5) and for the latent periods (fig. 6). The number of phase phenomena did not change under the influence of noise. Cases of clearly expressed negativism also attested to defectiveness of the excitation process during the period of exposure to vibration.

Prior to the onset of exposure the rat was completely adapted to the experimental conditions, and when placed in the conditioned reflexes chamber exhibited no defense reactions. After the onset of vibration the rat, when

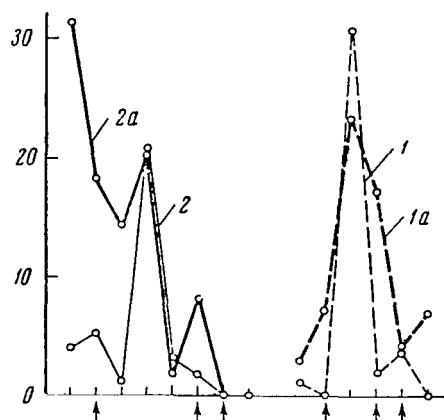


Figure 5. Effect of vibration and noise on mean value of conditioned reflexes in rat No. 4.

Along y-axis -- mean intensity of conditioned reflexes in relative units.
1a, 2a, Tone 1000 cps; 1, 2, light.

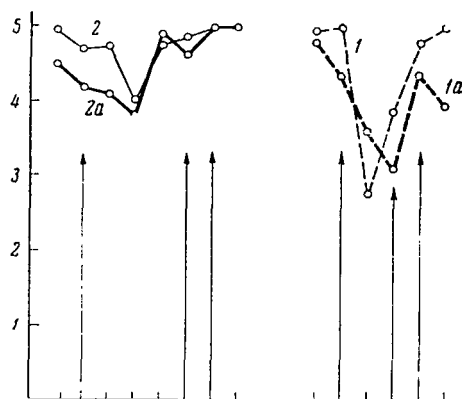


Figure 6. Effect of vibration and noise on mean latent periods of conditioned reflexes in rat No. 4.

Along y-axis -- mean latent periods of conditioned reflexes, in sec. Remaining notations same as in fig. 1.

placed in the chamber, or in the pauses between vibration, began to exhibit motor excitation, it attempted to escape from the chamber and became aggressive. During vibration there were seven cases of negativism, and only one such case in the period of exposure to noise. Once such a reaction was observed prior to an experiment with high conditioned reflexes. The distorted behavior of the rat can be regarded as a manifestation of the ultraparadoxical phase.

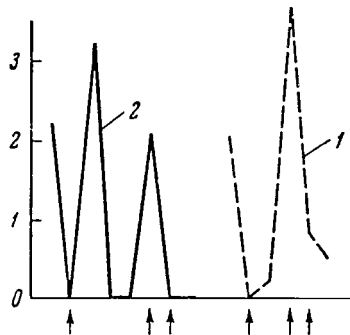


Figure 7. Effect of vibration and noise on differentiated inhibition of rat No. 4. Along y-axis--mean intensity of reaction to differentiation (tone 400 cps) in relative units. Remaining notations same as in figure 1.

These observations indicate the extreme inadequacy of the excitation ^{/78} process in this period as well. The brevity of the increase in conditioned reflexes is also indicative of this. The decrease in conditioned reflexes after the third exposure was accompanied by adjustment phases at a low level (fig. 5).

Discussion of Results

The mechanism of natural inhibition plays a significant and possibly a decisive role in the changes of conditioned reflexes caused both by the effect of noise and by the effect of vibration. Exposure to noise under experimental conditions is a well-known method for provoking natural inhibition. Vibration, as an extreme stimulus causing a sharp intensification of peripheral impulsation, can also create powerful natural inhibition. In the changes in conditioned reflexes during vibration which we observed, there were all characteristics typical of natural inhibition: in rats with a high initial conditioned reflex level the conditioned reflex level the conditioned reflexes decreased. In those cases with not very clearly expressed decrease of the conditioned reflexes, there was disinhibition of differentiation. In rat No. 4, due to the weakness of the principal nerve processes, the exposure to noise caused a state of protective inhibition. Z. N. Andreyeva (1964) pointed out that natural inhibition can cause disinhibition of protective inhibition. This phenomenon was observed in rat No. 4.

At the same time, there are appreciable differences between the effects of exposure to noise and combined exposure to vibration and noise.

The decrease in the intensity of the conditioned reflex to tone+ (strong stimulus) in the main group of rats, after exposure to the combination of these

factors, was sharper than after exposure to noise in all three exposures. The conditioned reflex to light after combined exposure decreased during the entire period of the exposures, but under the influence of noise the conditioned reflex decreased insignificantly and unreliably only at the beginning, and then exceeded the initial level. The difference between the total intensity of the conditioned reflexes in the experimental and control groups was statistically reliable even on the basis of our limited data.

Vibration in combination with noise exerted a sharply expressed generalized depression effect on positive conditioned reflexes, which persisted during all three exposures, at the same time that the depressing effect of noise was localized primarily in the auditing analyzer. Despite the fact that the increase in the conditioned reflex to light in the control group created conditions for the appearance of phase phenomena at a high level, the number of full adjustment and paradoxical phases increased insignificantly and unreliably, /79 whereas in the experimental group the increase in the number of phase phenomena was statistically reliable, and the disruption of the proper force relationships developed at a low level.

An increase in the number of phase phenomena was also observed in rat No. 4, despite the fact that according to other indices its reaction to vibration differed appreciably from the reactions of the rats of the main group. This gives us a basis for assuming that the inhibition caused by exposure to combined vibration and noise was protective inhibition. The results of our experiments agree with the data in the literature.

The distortion of the conditioned vascular reaction in human subjects during vibration can be interpreted as an ultraparadoxical phase (Butkovskaya, 1952, 1957a,b; Terent'yev, 1958, 1959). Phase phenomena in the cortex were also noted by authors who investigated the effect of vibration on the electroencephalogram (Shpil'berg and Mel'kumova, 1960; Volkov et al., 1960, and others).

Parabiotic phenomena in the lower parts of the CNS as a result of exposure to vibration have also been discovered by a number of investigators (Andreyeva-Galanina, 1956; Pavlova, 1958; Drogichina et al., 1961; Abramovich-Polyakov, 1962; Stoma, 1964; Kuznetsova, 1964a, and others).

Many authors correctly relate parabiotic phenomena to a sharp intensification of peripheral impulsation caused by exposure to vibration. The flow of impulses from the skin receptors, muscles, joints and the vestibular apparatus is excessive and causes parabiotic phases in the peripheral and lower parts of the CNS and protective inhibition in the cortex. In the functional changes induced by the effect of vibration in higher parts of the brain, an important role is played by the effect of vibration on the reticular formation of the midbrain. In rabbits, first injected with substances blocking cholinergic and adrenergic structures of the reticular formation, the effect of vibration did not cause stable changes in the bioelectric activity of the cortex and reticular formation (Andreyeva-Galanina, Artamonova, 1963). It is also possible to postulate participation of hormonal factors in this reaction, because during

exposures to vibration there was a change in the activity of the cortical layer of the adrenal glands. True, these phenomena were observed during more intense or prolonged exposures than used in our experiments (Tarasova, 1963; Sackler and Weltman, 1965).

Conclusions

1. The combined effect of vibration (70 cps, 0.4 mm, 15 min) and the noise of a vibration stand, with an intensity of about 75 db on conditioned reflexes and the effect of the noise component of this stimulus differ appreciably.

In the first case, in five of the six experimental animals there was a /80 generalized inhibition of the conditioned reflexes, and in the second a considerably less clearly expressed local inhibition in the auditory analyzer.

2. The changes in the conditioned reflex activity of rats arising during combined exposure to vibration and noise depend on the individual characteristics of higher nervous activity and initial conditioned reflex background.

In rats with a high level of conditioned reflexes there was development of protective inhibition. In rats with low-level conditioned reflexes there was disinhibition of conditioned reflexes and differentiations and phase phenomena.

Hypotheses on the mechanism of these phenomena are presented.

THE FUNCTIONAL SIGNIFICANCE OF CHANGES IN THE BIOELECTRIC ACTIVITY OF THE BRAIN AND ITS OXIDATING CAPACITY DURING VIBRATION

L. D. Luk'yanova and Ye. P. Kazanskaya

ABSTRACT

Exposure to whole-body vertical vibration (70 cps, 0.4 mm, 15 min) causes the appearance of a stable locus of excitation in higher regions of the CNS, accompanied by increased oxygen consumption and hypersynchronization of low-frequency oscillations in the EEG.

The phase of generalized excitation and the subsequent concentration of the excitation process are observed in the sensorimotor and visual regions of the cerebral cortex.

It is shown that the compensatory-adaptative mechanisms contributing to the decrease in sensitivity to vibration occur in connection with a decrease in excitation processes.

Presently the great sensitivity of the higher parts of the CNS to stimulation by vibration is completely obvious. We demonstrated earlier that even 1 min after onset of this stimulus, oxygen consumption changes sharply at different levels in the brain (Luk'yanova, 1964). For the purpose of broadening the possibilities for analysis of the observed changes and a broader understanding of the mechanism of the vibration effect, we conducted investigations of the bioelectric activity of the cerebral cortex and some subcortical structures, in addition to a study of oxidation processes. /81

In the relatively few studies devoted to an investigation of electroencephalograms (EEG) directly at the time of vibration (Volkov and Chirkov, 1955; Volkov, Kandaurova and Rumyantsev, 1960) it was noted that low-frequency vibration up to 50 cps can cause changes in the EEG in the form of a depression of the alpha rhythm, replaced with prolonged exposure to the stimulus (not less than an hour) by its rise, followed again by a decrease.

I. Ya. Borshchevskiy et al. (1963) investigated a wide range of frequencies (from 10 to 70 cps) with different amplitude characteristics, and discovered bioelectric changes arising in the brain during the period of exposure to vibration and unrelated to the frequency-amplitude characteristic of the latter. In the opinion of the authors, the changes were manifested either in an increase in the tonus of the excitation process (increased latent period of alpha waves during the closing of the eyes, replacement of the alpha rhythm by

a beta rhythm) or in an intensification of inhibition processes (more rapid appearance of alpha waves during the closing of the eyes). This study shows that exposure to stronger vibration parameters causes an intensification of inhibition during attenuation of the stimulation process. The authors note in individual cases the appearance on the EEG of slow waves with a frequency of 2-6 cps during and after vibration; they interpret these waves as confirmation of /82 intensification of the inhibition process in the brain.

In our study of the oxygen consumption and bioelectric activity of the brain, we exposed rats for 15-min intervals (repeated up to 30 times) to vertical vibration with a frequency of 70 cps and an amplitude of 0.4 mm. The method of polarographic determination of oxygen tension in the cerebral tissues is described in detail in a study by L. D. Luk'yanova (1964). The measurement of the maximum diffusion current in the investigated tissues and the recording of the EEG were done with the same bipolar electrodes. In the cortical parts of the brain we used a platinum needle electrode, 0.1 mm in diameter, with an un-insulated butt covered by a selective film and a silver chloride plate measuring

2.5 mm². This plate, in the case of measuring oxygen, was a comparison electrode and was inserted in a depression in the skull. The needle electrode, passing through the center of the plate, reached the surface of the cerebral cortex. For subcortical leads, two needle platinum electrodes with a diameter of 0.05 mm were placed at the center of the silver chloride plate. In this case the measurements of oxygen tension were made with one platinum and silver electrode, and the recording of the EEG was done with two platinum electrodes. The recording was done from the sensorimotor, visual and auditory regions of the cortex and from the caudate nucleus.

As in the earlier study, the value of oxygen consumption was judged from the change in oxygen tension (change of maximum diffusion current- I_{\max}) under

the influence of the "oxygen test" (passing a gas mixture containing 98-99 percent oxygen for 20 sec through the chamber in which the animal was placed). As a result of the increase in oxygen concentration, the increase in the maximum current caused by a change in oxygen concentration at the cathode (ΔI_{\max})

should be inversely proportional to oxygen consumption. Thus, in the case of intensive oxidation processes, the additional portion of oxygen is utilized rapidly, and the temporary increase in maximum current will be insignificant. With a depression of respiration the same "oxygen test" causes a considerable increase of I_{\max} , compared to the initial value. In an analysis of the changes

of the maximum current under the influence of the "oxygen test" in the earlier studies we made measurements of (1) the height of the maximum rise I_{\max} (h_{\max});

(2) the time of onset of the maximum of the increase I_{\max} (t_{\max}); (3) the time

of return of I_{\max} to normal (t_{ret}) and the latent period prior to the onset of the rise I_{\max} (fig. 1). However, careful analysis of the different parameters

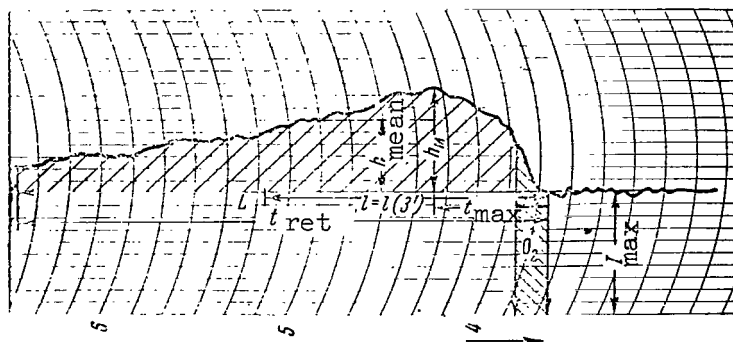


Figure 1. Change in oxygen tension (I_{\max}) during the "oxygen test." a, Area formed by change of I_{\max} with passage of oxygen through chamber (ΔI_{\max}); b, time during which oxygen is fed; h^m , maximum height of rise; t_{ret} , time of return of I_{\max} to normal; l , length of base of area ΔI_{\max} , equal to time during which it is measured (in this case, equal to 3 min); h_{mean} , mean height of measured area ΔI_{\max} .

determining the degree of changes in the maximum current revealed to us that a more precise and complete determination of the change $I_{\max} \rightarrow \Delta I_{\max}$ can be obtained by a planimetric measurement of the area ΔI_{\max} , formed by the change of I_{\max} during and after passing oxygen through the chamber (fig. 1).

It is still more convenient to use a value which has a strict proportional dependence on ΔI_{\max} --the mean height of the measured area (h_{mean}); then $\Delta I_{\max} = S_{\Delta I} / h_{\text{mean}}$, where l is the length of the base of the area, equal to the time during which the area is measured (in this study it was always computed for a time of 3 min).

The electrical activity of the brain was recorded using a four-channel 4EEG-1M amplifier with pen recorder. At the time of the experiment the animal was free in the screened chamber, fastened to the vibration stand.

Investigation of the values ΔI_{\max} and h_{mean} prior to exposure to vibration revealed that at the norm, beginning with the second-third measurement, good

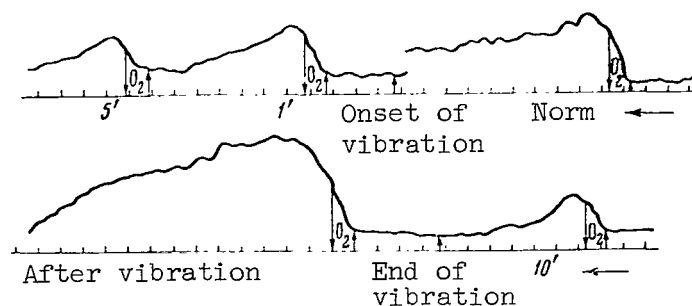


Figure 2. Dynamics of changes ΔI_{\max} during and after stimulation by vibration.

reproducible results were obtained. Some differences in the first measurements, in the direction of a decrease or increase of ΔI_{\max} (or h_{mean}), in comparison with later measurements, apparently were caused by the orienting reaction of the animal to its surroundings and later decreased with increased stay.

However, the first vibration, as we mentioned, caused a sharp decrease in ΔI_{\max} , and accordingly in its area ($S_{\Delta I}$) and h_{mean} , whereas after vibration these values increased in comparison to normal (fig. 2).

As pointed out in our earlier studies, multiple exposure to vibration, ^{/84} when applied daily, led to an increase in the duration of the phase of increased oxygen consumption of cerebral tissues. Among the rats investigated in this study the oxygen consumption during vibration changed much as indicated previously. With an increase in the number of exposures above 20, this first response reaction was maintained.

Thus, increased oxygen consumption during exposure to vibration, observed in the overwhelming majority of cases in all parts of the brain, is a specific response of brain tissues to this stimulus.

However, analysis of the bioelectric activity of the brain of animals at the time of vibration made it possible to define two main periods characterizing the response reaction to exposure.

The first period, extending up to 4-8 (in different rats) vibrations, was related to the appearance of the most sharply expressed changes in the EEG.

In response to the effect of the first vibration period, we found an orienting reaction, apparently depending on the initial functional state of the animal. It was expressed in the form of desynchronization, or synchronization

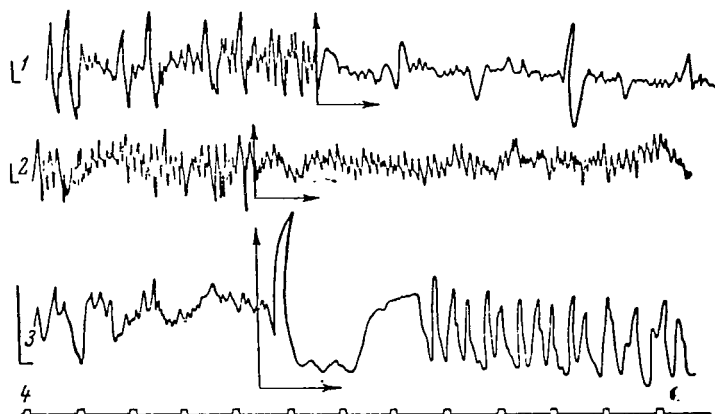


Figure 3. Different forms of bioelectric activity in response to first stimulation by vibration. 1, Desynchronization; 2, synchronization; 3, hypersynchronization; 4, time reading in sec. Arrow denotes onset of vibration.

or hypersynchronization of the bioelectric activity (fig. 3). The most common was the first type of reaction. Similar forms of appearance of the orienting reflex to an indifferent stimulus were noted by R. S. Mnukhina (1964), who believes that at the intermediate level of the functional state of the cortex the indifferent stimulus causes an orienting reaction in the form of desynchronization; with a decrease in the functional state of the cortex this same indifferent stimulus causes an orienting reaction in the form of diffuse synchronization of rhythm. In animals whose cortex is characterized by a relatively low level of lability, the orienting reaction is manifested most frequently in the form of hypersynchronization of rhythm. /85

Further changes in the EEG under the influence of vibration apparently depend on the relations of the excitation and inhibition processes in the animals. However, it is possible to define the basic general patterns in the development of the response reaction in this period.

The first vibration stimulus caused a very rapid (after 30-60 sec) appearance in the sensorimotor and visual regions of the cerebral cortex activity, alternately arising in connection with the orienting reaction of the animal: hypersynchronized, low-frequency (1-3 cps) and high-amplitude (500-700 μ V) oscillations with or without superposed high-amplitude rhythms (fig. 4). In the caudal nucleus at this time there usually was a stable desynchronization of rhythm with indistinct appearance of slow oscillations, intensifying somewhat by the 15th min of vibration. In the auditory region of the cortex slow oscillations were also expressed considerably more weakly.

However, even the 2nd-3rd vibration revealed a gradual generalization of the slow hypersynchronized oscillations in all investigated regions, especially clearly expressed at the end of vibration (fig. 5). An intermediate form of

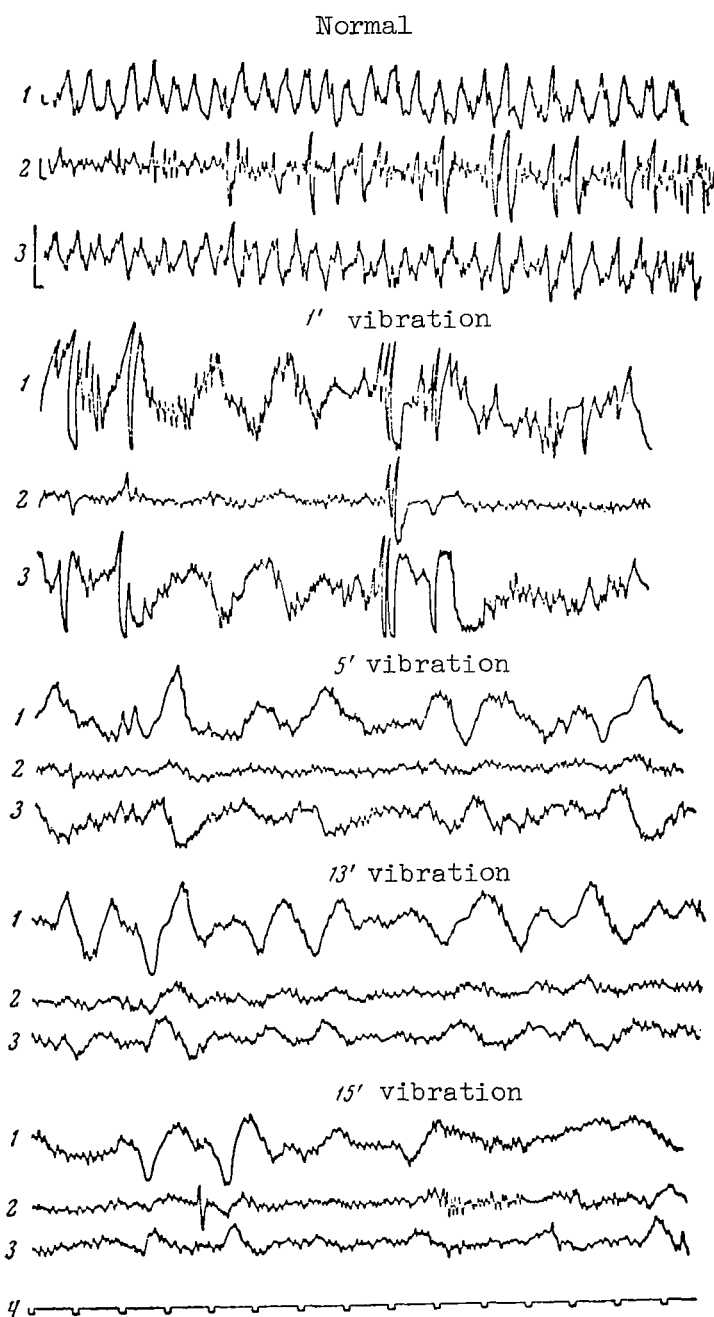


Figure 4. Changes in bioelectric activity during time of first vibration in rat No. 9. 1, Sensorimotor region of cortex; 2, caudate nucleus; 3, auditory region of cortex; 4, time reading in sec.

Normal

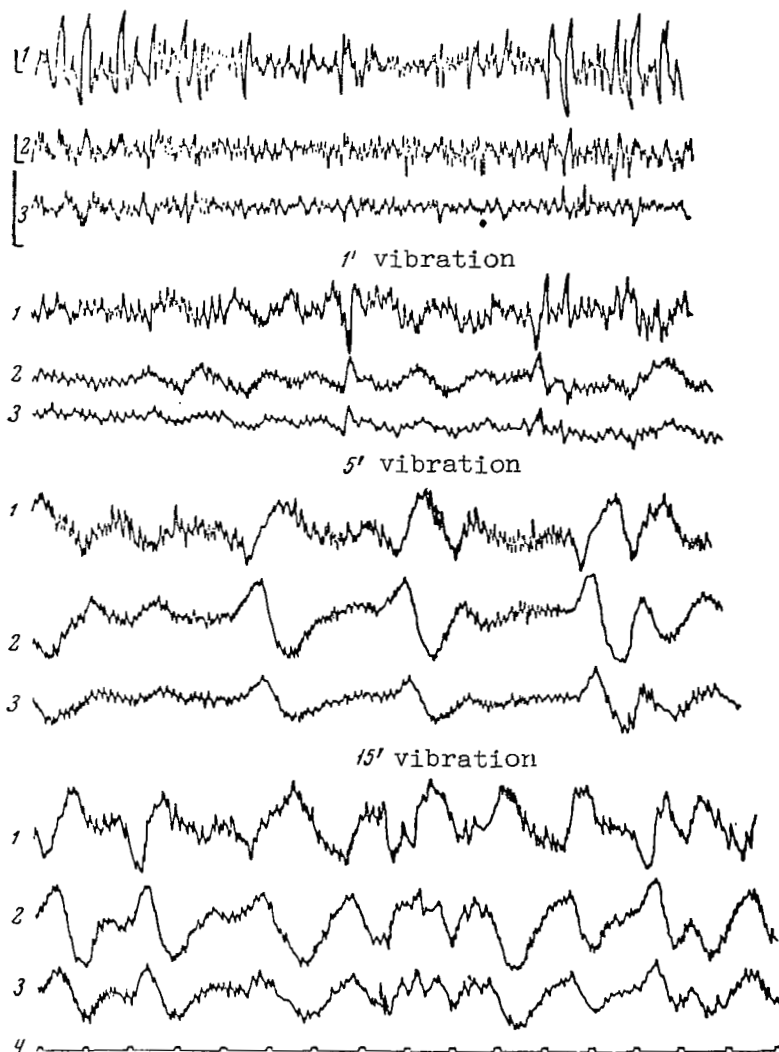


Figure 5. Changes in bioelectric activity during second vibration in rat No. 9.

1, Sensorimotor region of cortex; 2, auditory region of cortex; 3, caudate nucleus; 4, time reading in sec.

activity, frequently observed in animals with an obviously lower sensitivity to vibration, was a synchronized rhythm of 6-7 min, superposed on slow waves 88 of considerably lesser amplitude than the hypersynchronized oscillations mentioned above (fig. 5). In the course of the first few vibrations there was a gradual increase of the amplitudes of these slow oscillations, their earlier appearance and complete disappearance of rapid activity.

Finally, we observed a state wherein slow hypersynchronized high-frequency oscillations, frequently assuming a sinusoidal form, appeared almost instantly, but were localized for the most part in the sensorimotor and visual regions of the cortex. In the auditory region of the cortex and in the motor region of the subcortex they were expressed far more clearly. Here there frequently was a burst-like, spindle-like form of activity and synchronized rhythms of 10-12 sec (fig. 6). These changes all occurred approximately in the course of the first 6-8 exposures to vibration.

Taking into account that these changes in the bioelectric activity of the brain developed against a background of a sharp and generalized increase in oxygen consumption in these same sectors, we assume that the appearance of high-amplitude, low-frequency hypersynchronized sinusoidal oscillations with a frequency of 1 cps during vibration is a reflection of a stable and extremely strong center of excitation in higher parts of the CNS.

Moreover, we noted that maximum oxygen consumption in the cerebral tissues usually coincided with the appearance in the sensorimotor and visual regions of the cortex of smooth, sinusoidal, hypersynchronized oscillations. Prior to the onset of this moment, that is, in the period preceding maximum oxygen consumption in the cerebral tissues, the EEG showed transitional types of harmonics, even including a brief slow arrhythmia (bradyrhythmia)¹. In some of the animals in the first 1-2 exposures to vibration the excitation phase, judging from the oxygen test, was unclearly expressed. In this case the high-amplitude stationary oscillations did not appear at all, and the bioelectric activity of the cortical parts was characterized by synchronous, relatively low-frequency rhythms, persisting stably during the entire course of vibration with a periodically appearing negative change in the constant potential.

Thus, the hypersynchronized slow oscillations with a period of 1 cps apparently corresponded to the appearance of centers of overexcitation under stress stimuli. If this is the case, their initial appearance at the cortical end of the kinesthetic analyzer becomes more understandable, because this part apparently should be the most sensitive to the vibration stimulus. A less clear role is played by the visual end of the cortical analyzer in the development of the response reaction to vibration. However, data are available which support the idea that the conductors of vibration sensitivity in the brain run close to the conductors of pain and thermal sensitivity, reaching the parietal lobe and also the frontal and posterior central convolutions (Petelin, 1931; Demarina, 1954).

On the basis of these fragmentary samples it also follows that the auditory end of the cortical analyzer plays a considerably lesser role in the perception of the stimulating impulsation accompanying vibration.

¹The oscillations recorded in this period have a sawtooth appearance, due to superimposition on the low-frequency waves of more rapid synchronous rhythms, which disappeared with continuing development of the process.

Normal

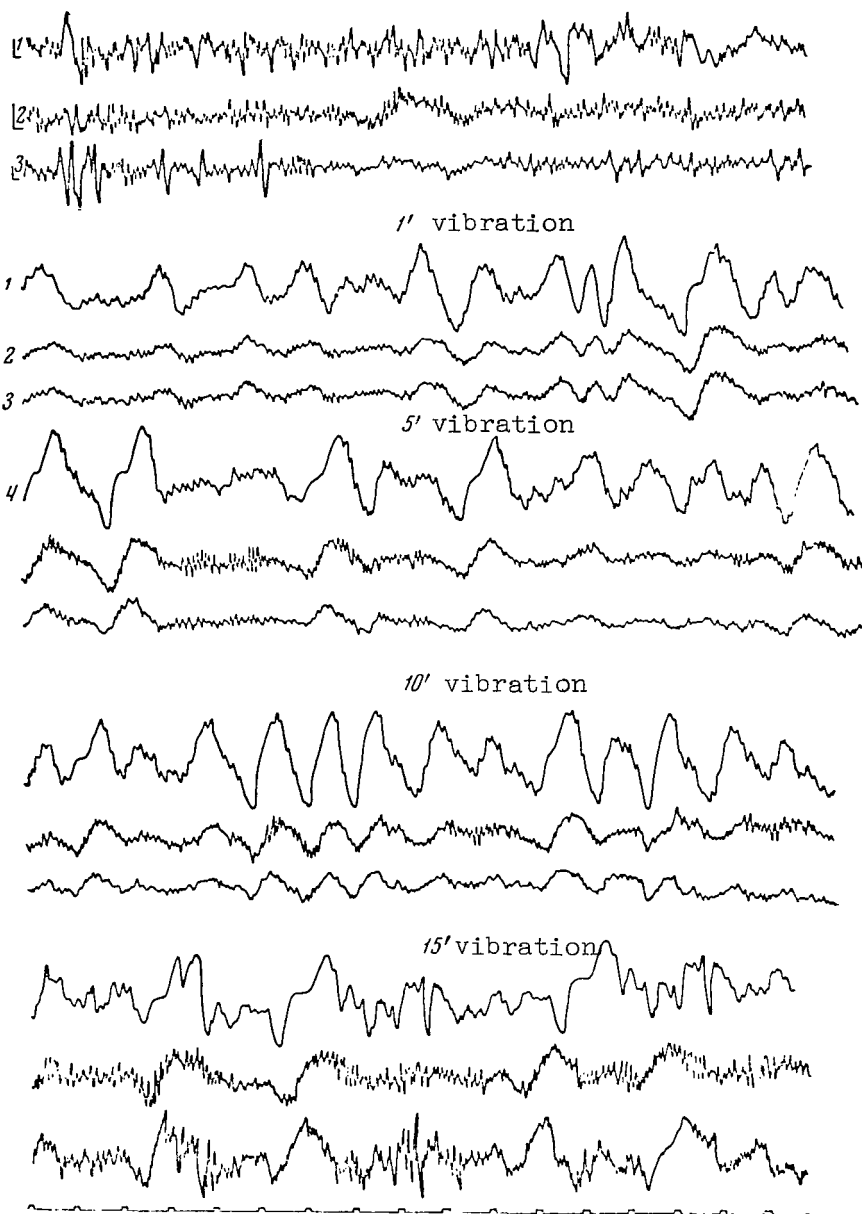


Figure 6. Changes in bioelectric activity during the sixth vibration in rat No. 9. Notations same as in figure 4.

From the point of view of the general effect of a vibration stimulus on different parts of the brain, there is a general biologically responsive, regular reaction of the nervous system to an indifferent stimulus, characterized by initial excitation of centers associated with the effect of this stimulus,

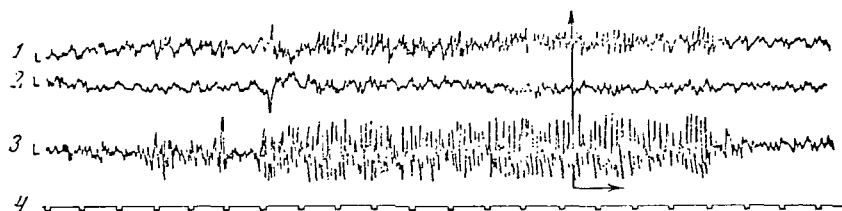


Figure 7. Example of bioelectric activity at onset of 23d vibration. 1, Sensorimotor region of cortex; 2, visual region of cortex; 3, caudate nucleus; 4, time reading in sec.

generalization of excitation into other parts, and secondary concentration of the excitation process in strictly localized zone.

The first two stages are included in the initial period of the most active reaction of the animal to vibration which we defined, in which after a 15-min exposure as a result of an extraordinarily strong overexcitation of nervous centers in the higher parts of the brain, there usually appears a clearly expressed protective inhibition. (Postvibration decrease of oxygen consumption, changes in the EEG of the animal, characteristic of complete extinction of the conditioned reflexes in the first few hours after cessation of vibration.) Upon completion of vibration the animal usually lies stretched out on the bottom of the chamber with relaxed muscles, completely indifferent to its surroundings (L. D. Luk'yanova, A. V. Kol'tsova, Ye. S. Meyzerov, Ye. P. Kazanskaya, p. 99).

Thus, in this case there is direct confirmation of the opinion of A. B. Kogan (1958) that slow waves may not reflect inhibition itself, but the propagation of a process of excitation leading to inhibition.

The second stage, which we called the period of relative normalization of the reactions of the animal in response to stimulus by vibration, was characterized by a prolonged state and variability. It began after 4-8 vibrations and persisted during the entire subsequent period of the investigation. In this period there was a gradual decrease or complete disappearance of the response occurrence of the orienting reaction to vibration (fig. 7), and an increase in the latent period of development of slow hypersynchronized high-amplitude oscillations, being localized increasingly in the sensorimotor and visual regions of the cerebral cortex. The dominating rhythms in the auditory region of the cortex and in the motor region of the subcortex were low-frequency (8-12 oscillations/sec) synchronized rhythms with considerably lower amplitude, superimposed on slow low-amplitude oscillations. There was an increase of burst-like, spindle-like activity. This form of activity also disappeared gradually, and was then replaced by the suppression of the rhythm. At the end of this period individual days could be observed in which the suppression of rhythm, appearing in the background activity, also persisted at the time of vibration (fig. 8). The appearance of slow waves of considerably lower

Normal

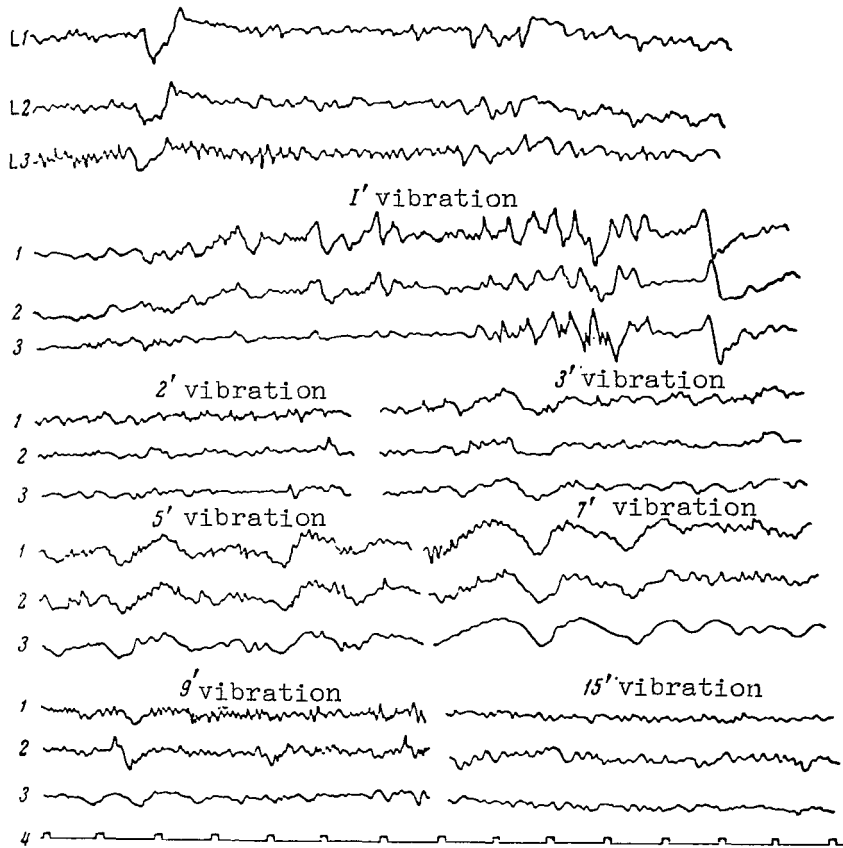


Figure 8. Changes in bioelectric activity in rat No. 23 during the 25th vibration. Notations same as in figure 7.

amplitude than in the cases described was brief and was replaced by low-amplitude oscillations. The suppression of rhythm was manifested most clearly in the sensorimotor region of the cortex and in the motor region of the sub-cortex. These phenomena indicate a decrease in the sensitivity of the higher parts of the brain to stimulation by vibration in the second period. In view of the data presented in the article by L. D. Luk'yanova, A. V. Kol'tsov, Ye. S. Meyzerov and Ye. P. Kazanskaya, these facts may also be evidence of decreased excitability of the nervous system as a result of multiple vibration.

Investigation of the electrical activity of the brain during vibration, within the limits of the investigated periods, did not make it possible to detect the onset of a third period, in which the reaction to vibration would be completely absent. It was mentioned above that with a general decrease in the level of bioelectric activity in the investigated parts of the brain, including the last vibration, there were days when in response to exposure to

vibration a reaction developed, which was typical for the first period or the onset of the second. Thus, despite the daily application of vibration during an entire month, an instability of nerve processes continued to occur at the time of the exposure itself. These data do not make it possible to speak of the strength of compensatory-adaptative phenomena in this period. The possibility of their occurrence against a background of sharp and long-persisting decreases in excitability of the higher parts of the brain is too great an expense to the organism. In order for the animal to virtually cease to react to the effect at the time of the vibration itself, this decrease would apparently have to be particularly intense. It is entirely possible that at this stage it would border on the development of a pathological, irreversible process in the higher parts of the brain. /92

Thus, a complex picture prevails, in which mechanisms facilitating a decrease in the vibration effect may appear only due to disruption of normal interrelations between stimulation and inhibition processes by functional rearrangement of the activity of the higher parts of the brain with a transition to a lower level. In the bioelectric activity of the brain of different animals there are deviations from this scheme toward a change in the times of onset of any stage, and also in the sense of prevailing low-frequency, high-amplitude oscillations or synchronized, low-amplitude, high-frequency rhythms with burst activity superimposed on them. However, the general trend of the process was maintained in all animals. Slow sinusoidal oscillations were observed in 100 percent of the cases. In two cases, at the time of vibration, high-amplitude generalized spikes were noted on the EEG.

It should be noted that the reaction to vibration of such small animals as a rat, judging from the picture of bioelectric activity, is higher than in man exposed to identical parameters. It was pointed out above that the depression of rhythm and the appearance of slow waves with a frequency of 2-6 cps were noted by investigators in human subjects only in individual cases and after far longer exposure to vibration. The difference in the observed effect could depend both on the "density" of the vibration per unit weight of the body, and on the specific effects of vibration on receptors in different organisms. This phenomenon can be of great importance in the development of space flights, because it obviously becomes necessary to carry out a detailed investigation of the individual and species differences in the response reaction to vibration.

Summarizing the general results of these processes, the following main points should be distinguished.

1. Vibration stimulus at the time of exposure leads to the appearance in higher parts of the CNS of a stable center of excitation, accompanied by an increase in the level of oxygen consumption and appearance of hypersynchronized, low-frequency sinusoidal oscillations with a frequency of 1 cps.

2. As the number of vibration exposures accumulates, the phase of increased oxygen consumption (excitation phase) expands with time, and is accompanied by definite changes in the bioelectric activity of the brain, making it possible to suppose that compensatory-adaptative mechanisms appear during this period. /93

3. These compensatory-adaptation mechanisms, facilitating decreased sensitivity to vibration in animals, arise in connection with a decrease in excitation processes.

4. The change in oxygen metabolism of the brain toward its increase (increase in oxygen consumption by cerebral tissues) is not always accompanied by uniform changes in the bioelectric activity of the brain.

5. The changes in the bioelectric activity of the brain at different levels at the time of exposure to vibration allow us to speculate on the presence of a phase of generalized excitation, irradiating to different parts of the brain, and phases of concentration of the excitation process in definite zones of the cerebral cortex (sensorimotor and visual cortex).

EFFECT OF VIBRATION STIMULUS ON THE OXYGEN METABOLISM OF THE
BRAIN IN ANIMALS WITH PARTIALLY ELIMINATED
AUDITORY AND VESTIBULAR SYSTEMS

L. D. Luk'yanova and S. M. Ambrosova

ABSTRACT

Rats were exposed to repeated whole-body vertical vibration (70 cps, 0.4 mm, 15 min). Oxygen consumption in different parts of the brain was studied.

It was shown that partial destruction of the vestibular apparatus contributes to the appearance of compensatory-adaptation effects on the indices, without a decrease in the general functional level of the CNS.

In experiments on anesthetized animals direct proof was obtained of the extremely important role of the vestibular apparatus in the perception of vibration.

In our earlier investigations we demonstrated that oxygen consumption ^{/95} in the cerebral tissues of animals subjected to vibration sharply changes (Luk'yanova, 1964). We also found that there is a dissimilarity in these changes in different parts of the brain. Further investigation of the mechanism of the effect of vibration on the CNS requires careful study of the functional significance of different regions of cortical analyzers and subcortical formations associated with them in the development of a response reaction to this stimulus.

In the literature there are many indications to the effect that vibration can be a strong, adequate or inadequate stimulus of the organ of equilibrium (Kulikovskiy, 1939; Voyachek, 1946; Usenko, 1961; Shpil'berg, 1960, and others).

The opinion prevails that the otolith of the sacculus possesses a specific sensitivity to stimulus by vibration (Yazykov, 1951; Kostrov¹; Usenko, 1961). However, it is noted that low-frequency vibration to 20 cps exerts a stimulating effect on the semicircular canals. High frequencies act on the nonauditory part

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Reference is to Borshchevskiy et al., 1963.

of the labyrinth apparently as inadequate stimuli (Zagryadskiy, 1957; Usenko, 1961; Andreyeva-Galanina, 1963). However, many investigators relate the vestibular disruptions observed during vibration not so much to changes in the peripheral labyrinth as to formation of a pathological process in the central paths and structures of the vestibular analyzer and in its relationships to other analyzer systems (Voyachek, 1946; Usenko, 1961; Zagryadskiy, 1957; Shpil'berg, 1960, 1962, and others).

Specifically for this reason it is therefore of particular interest to study the influence of vibration on the function of the higher parts of the 96 CNS in the case of destruction of the peripheral end of the vestibular apparatus, on the one hand, and with destruction of different parts of the cortical analyzers, on the other. In the literature familiar to us there are no reports on attempts to make such investigations.

Research Method

Male Wistar rats, weighing 200-250 g were used. Oxygen in the cerebral tissue was determined by the polarographic method. The details of the use of this method under chronic conditions as applied to rats in a free state are preserved in a study by L. D. Luk'yanova (1964). The changes in oxygen consumption in the investigated parts of the brain were judged on the basis of the change in maximum diffusion current under the influence of the "oxygen test" (ΔI_{\max}) using the same method as described in a study by L. D. Luk'yanova and Ye. P. Kazanskaya (p. 75). We mention only briefly that the value ΔI is inversely proportional to the level of oxygen consumption in the investigated tissue. Therefore, a decrease in ΔI_{\max} indicates an increase in the consumption of oxygen, whereas increase of ΔI_{\max} indicates a decrease.

First, using intact animals, a careful study was made of the change in oxygen consumption under normal condition and during vibration (three-four exposures). Then the outer and middle auditory apparatus was destroyed surgically (breaking of the drum membrane and removal of the earbones). Thereafter a study was made of the change in oxygen consumption during and after vibration. Finally, in these same animals, the otolithic organs were destroyed surgically. It should be noted that in most rats there was virtually no external manifestation of a reaction. In only 20 percent of the animals were there insignificant visible deviations from normal (paws deflected to one side, uncertainty of movements, creeping, impairment of choice of a linear direction and its replacement by circular, rotational movement). However, these changes appeared only on the first few days after the operation and later disappeared. The use of methods of destruction of the vestibular apparatus by other investigators (chloroform, iodoacetic acid), following their administration, did not in general lead to any visible changes. The effect of chloroform in large quantities (not several drops, but

0.5-1.0 cm³) caused, as will be demonstrated below, an intense narcosis

affecting the entire cerebral cortex of the animal. Upon termination of its effect the animal did not differ from other intact animals. The absence of 97 apparent changes in the motor reaction in rats with a removed vestibular apparatus could be an expression of compensatory adaptations. In such a case the additional functional loads associated with the activity of this apparatus should make these disruptions obvious.

The investigation of the oxygen metabolism was carried out in the sensorimotor and auditory regions of the cortex, in the caudate nucleus, in the reticular nucleus of the thalamus and in the cortex of the cerebellum.

All animals were exposed to 15 min of vibration with a frequency of 70 cps and an amplitude of 0.4 mm.

Experimental Results

Influence of Vibration on Oxygen Consumption in Different Parts of the Brain of Intact Rats

The investigations confirmed earlier data to the effect that in all experimental intact animals during response to exposure to vibration, changes in oxygen consumption take place in three phases: (1) increased oxygen consumption, already occurring at the time of vibration, with maximum changes taking place at the 5th minute of vibration (decrease of ΔI_{\max}); (2) decreased oxygen consumption, developing immediately after termination of vibration, and (3) gradual restoration to the initial level. The second period is apparently a reflection of protective inhibition developing in the higher parts of the brain (Luk'yanova, 1964) and has two maxima. The first, most clearly expressed period, associated with a sharp decrease in oxygen consumption immediately after vibration (increase of ΔI_{\max}), sets in 15-20 min after vibration; the second, 1.5-2 hr later (fig. 1).

Some deviations from this pattern were observed in an investigation of oxygen consumption in the reticular nucleus of the thalamus and in the cortex of the cerebellum. In these regions the period of increased oxygen consumption, developing already at the time of vibration, was far more prolonged than in the other investigated parts (30-45 min). For this reason an inhibited state developed at far later times (cortex of the cerebellum) and could be expressed exceptionally insignificantly (reticular nucleus of the thalamus).

Influence of Vibration on Oxygen Consumption in Different Parts of the Brain of Rats with a Partially Destroyed Auditory Apparatus

Partial impairment of hearing by destruction of the outer and middle auditory apparatus led to a decrease in changes of ΔI_{\max} after vibration in the

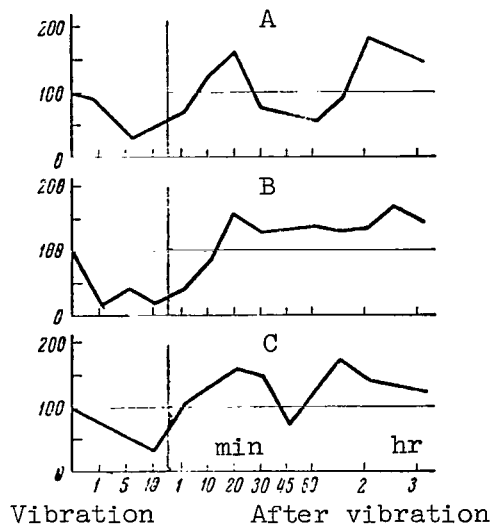


Figure 1. Change of ΔI_{\max} values during and after exposure to vibration. A, In sensorimotor region of cortex; B, in motor region of subcortex; C, in auditory cortex. Along x-axis -- time in minutes; along y-axis -- value Δ_{\max} in percent of initial background.

auditory region of the cortex, in the caudate nucleus and in the reticular ⁹⁸nucleus of the thalamus, compared to the intact animals, and to an increase of ΔI_{\max} in this same period in the sensorimotor cortex (figs. 2 and 3). Virtually no changes were observed in the cortex of the cerebellum.

Thus, partial destruction of hearing apparently attenuated the flux of the stimulating impulsation transmitted to the cortical end of the auditory analyzer in this connection decreased the exciting effect of vibration, and therefore did not cause overexcitation of the nerve cells in this region, leading to the appearance of subsequent inhibition. The parallelism between the observed picture in the auditory region of the cortex and in the caudate nucleus makes it possible to postulate the presence of direct connections and relations between these regions. The different direction of the process in the sensorimotor cortex can be interpreted as a manifestation of negative induction between this region and the auditory cortex, in which the decrease of the functional activity of one of them (auditory) leads to increase of excitation in the other (sensorimotor). In this case the vibration stimulus inevitably should lead to a more clearly expressed overexcitation of the nerve cells and therefore to a more intense subsequent protective inhibition.

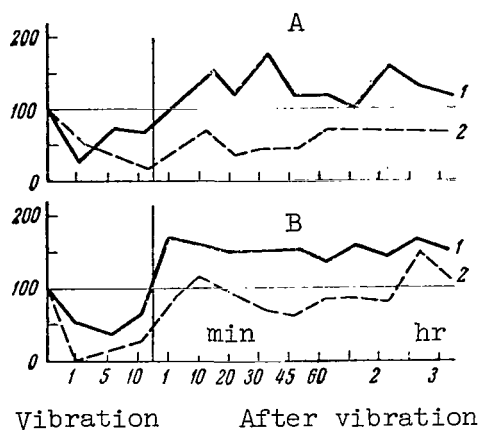


Figure 2. Change of ΔI_{\max} values in the auditory region of the cortex in intact animals (1) and in animals with partially destroyed hearing (2) during and after vibration. A, Rat No. 17; B, Rat No. 16. Other notations same as in fig. 1.

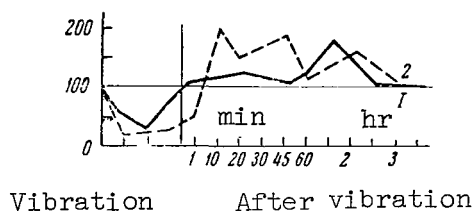


Figure 3. Change of ΔI_{\max} values in the sensorimotor region of cortex of rat No. 15 (under influence of vibration) before (1) and after (2) partial destruction of hearing. Notations same as in fig. 1.

Influence of Vibration on Oxygen Consumption in Different Parts of the Brain in Rats with a Partially Destroyed Vestibular Apparatus

An investigation of oxygen consumption in different regions of the brain in the animals of this series revealed that their reactions to the initial 199 and subsequent vibrations were different. For example, in the cortical end of

the auditory analyzer the direction of change of oxygen consumption after application of the first vibration did not change compared to animals in which only one external auditory apparatus was destroyed.

In the sensorimotor region of the cortex the excitation phase (related to an increase in oxygen consumption) after the first vibration was expressed less clearly than in the intact animals and in animals with a destroyed external auditory apparatus. In individual cases there was even decrease in oxygen consumption during vibration in comparison with the norm. The inhibition developing after vibration was considerably greater in its depth and duration than this phase in the intact animals (an appreciable increase in ΔI_{\max} compared to the norm). In the caudate nucleus, reticular nucleus of the thalamus, and cerebellum the first exposure to vibration in the animals of this series led to a prolonged postvibration increase in oxygen consumption (decreased ΔI_{\max} compared to the norm).

The latter can be regarded as a decrease in excitation in these parts during this period, apparently related to the limitation of the impulsation earlier transmitted from the vestibular apparatus into these regions of the brain. For this region, subsequent inhibition did not develop.

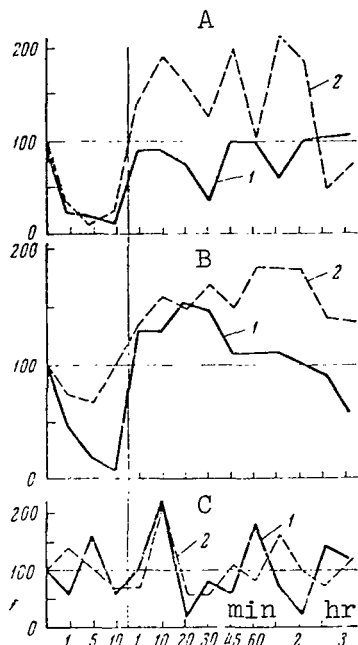
With respect to the sensorimotor region of the cortex, here, as in the case with destruction of the auditory apparatus, there apparently is increased excitability of nerve cells, leading to clearly expressed subsequent overexcitation. This in turn demonstrates a close functional interrelationship between the vestibular and sensorimotor cortical analyzers.

During subsequent daily vibrations of animals with a partially destroyed vestibular apparatus there was a period of considerable intensification of the second phase compared to intact animals and a period of relative normalization.

In the auditory end of the cortical analyzer this process was expressed more clearly than in the other regions of the brain. It did not set in immediately and did so only after at least three periods of vibration; it was characterized by instability. In the course of the entire investigated period we did not observe stable normalization in this region.

In the sensorimotor region of the cortex and in the motor region of the subcortex (caudate nucleus), the decrease in oxygen consumption after multiple application of the stimulus, expressed in an increase in ΔI_{\max} , considerably

exceeded these same changes in intact animals (fig. 4). As in the auditory region, this process had a clearly expressed oscillatory character not only on different days, but even in the course of a single experiment. However, on the 8th-10th days, with continuing daily vibration, a new state was discovered, in which the phase character in oxygen consumption during and after vibration, customary for intact animals, disappeared and only irregular fluctuations of ΔI_{\max} near normal remained (fig. 4).



Vibration After vibration

Figure 4. Change of ΔI_{\max} values in sen-

sorimotor region of the cortex during multiple vibration in animals with partially destroyed auditory and vestibular apparatus (rat No. 15).

A, First (1) and second (2) vibrations after destruction of the vestibular apparatus;
B, fifth (1) and sixth (2) vibrations;
C, 11th-12th vibrations (1, 2). Other notations same as in fig. 1.

These data indicate that destruction of the vestibular analyzer causes serious disruption of normal cortico-subcortical interrelationships.

The difference between the response reactions for oxygen consumption on the first day of vibration for animals of this series and in the subsequent period indicates the appearance on the first day after destruction of the otoliths of temporary compensatory adaptations which are easily disrupted during vibration and its aftereffect. Repeated applications of vibration apparently lead to an increase in the excitability of the sensorimotor region of the cortex and the motor region of the subcortex. Extreme instability in cerebral /101 activity appears. Judging from oxygen consumption, the states of inhibition and excitation very rapidly replace one another, something not observed in intact animals.

This is evidence of complex competition between the inhibition and excitation process concentrated for the most part in sections through which a

particularly strong flux of impulsation should pass during vibration. Obviously, in this period it is in these sections where there is formation of new compensatory mechanisms capable of restoring the cortico-subcortical relationships disrupted at the time of destruction of the vestibular apparatus. The phase of relative normalization in the animals of this group differed from that for intact animals. Whereas in the latter the decrease of sensitivity to vibration occurred due to a general decrease in the excitability of higher parts of the brain, upon destruction of the otoliths and after compensatory adaptations possibilities apparently arose for adaptation to vibration without a decrease in the general functional level. This can explain the absence of a phase character in oxygen consumption already by the 8th -10th vibrations, that is, the absence in higher parts of the brain of centers with clearly expressed excitation and overexcitation. Thus, there is also a decrease in sensitivity to vibration here. However, while in intact animals this was attained by a general progressive decrease in the excitability of all parts of the brain which could not but be reflected in its general functional state, in the latter case the animal body could dispense with such an extreme measure.

Influence of Vibration on Oxygen Consumption in the Cerebral Tissues of Anesthetized Animals

In this series of experiments the animals subjected to vibration were in the second or third stage of ether narcosis. In this case the oxygen consumption decreased in all investigated parts of the brain. However, the most prolonged effect of ether narcosis was on the cortical section, where there was a clearly expressed secondary decrease in oxygen consumption, coinciding with a period of secondary sleep (60-90 min after onset of the effect of the narcosis, fig. 5). Chloroform, introduced through the outer auditory meatus (0.5-ml), exerted a narcotic effect on the investigated parts of the brain similar to that of ether (fig. 6).

Partial destruction of the vestibular apparatus did not change the reaction of the animals to anesthesia.

In the study of the effect of vibration on anesthetized animals, the latter were first put under general anesthesia until the wink reflex disappeared, and were then exposed to vibration.

Figure 7,B shows that the oxygen consumption in intact anesthetized animals increases sharply under the influence of vibration (decrease of ΔI_{\max}), and in individual cases may even assume a phase character, typical for

vibration, but somewhat less clearly expressed in amplitude in the case of a less strong preliminary anesthetization of the animals (fig. 7,A). A different effect is observed in anesthetized animals with destruction of the vestibular apparatus. The disinhibiting effect is observed considerably later, or does not appear at all (fig. 8).

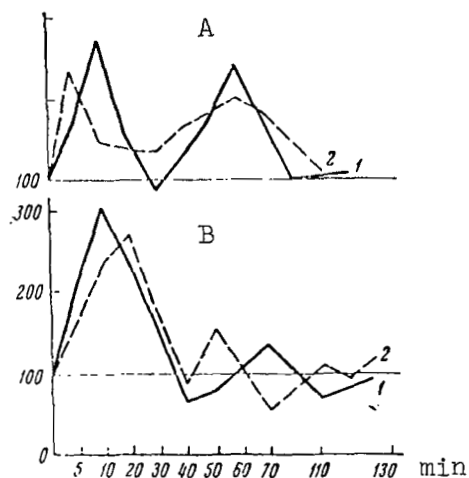


Figure 5. Change of ΔI_{\max} values in rats

not subjected to vibration during ether narcosis.

A, In sensorimotor region of cortex;

B, in motor region of subcortex; 1, rat No. 19; 2, rat No. 18.

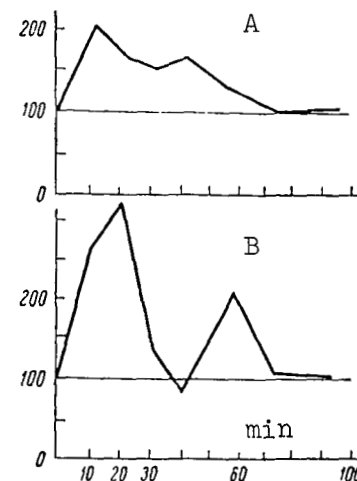


Figure 6. Change of ΔI_{\max} values in rats

not subjected to vibration during chloroform narcosis.

A, In motor region of subcortex, B, in sensorimotor region of cortex. Other notations same as in fig. 1.

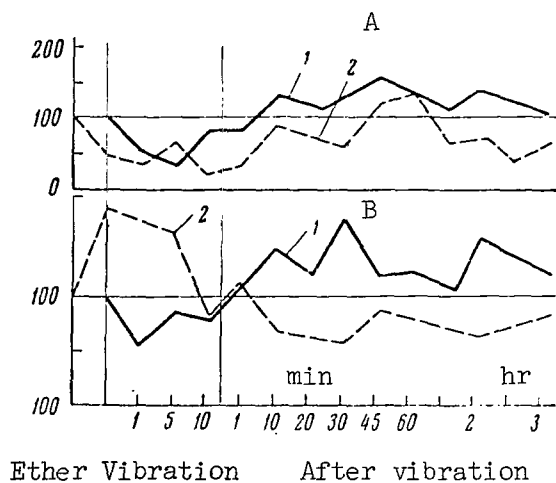


Figure 7. Change of ΔI_{\max} values in motor region of subcortex during and after exposure to vibration against background of ether narcosis. A, Changes of ΔI_{\max} against a background of shallow ether narcosis; B, changes of ΔI_{\max} against background of intense ether narcosis; 1, changes of ΔI_{\max} in animal without ether narcosis; 2, changes of ΔI_{\max} in same animal with ether narcosis.

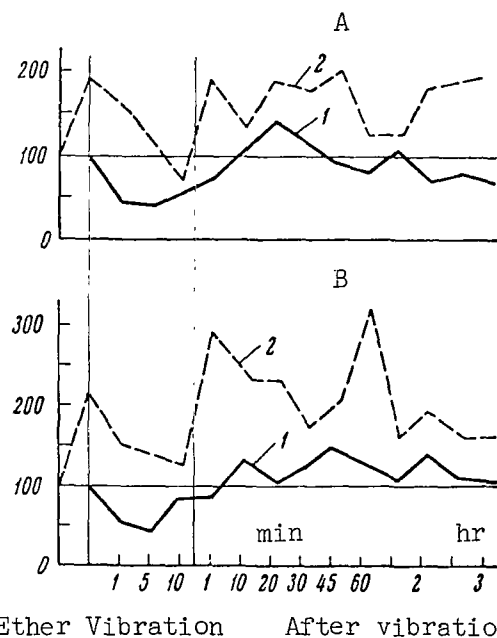


Figure 8. Change of ΔI_{\max} values during and after exposure to vibration in animals with a partially destroyed auditory and vestibular apparatus during ether narcosis. A, In sensorimotor region of cortex; B, in motor region of subcortex; 1, intact animals; 2, with ether narcosis.

Thus, these experiments are a direct demonstration of the extraordinarily important role of the vestibular apparatus (otoliths) in the perception of vibration stimuli and in those processes which develop in different parts of the CNS under the influence of vibration.

Conclusions

1. The partial destruction of the auditory apparatus in rats decreases the stimulating effect of vibration in the auditory region of the brain, in the caudate nucleus and in the reticular nucleus of the thalamus, and increases its effect in the sensorimotor region of the cortex. /104
2. Preliminary partial destruction of the vestibular apparatus in rats subjected to vibration leads to decreased oxygen consumption in the sensorimotor region of the cortex and in the caudate nucleus compared to intact animals.
3. Vibration stimulation of intact animals against a background of ether or chloroform narcosis exerts a disinhibiting effect and restores oxygen consumption in cerebral tissues to the usual level observed in nonanesthetized animals.
4. Vibration of anesthetized animals with a partially destroyed vestibular apparatus does not exert an appreciable disinhibiting effect on oxygen metabolism.

INVESTIGATION OF THE RELATIONSHIP BETWEEN THE OXYGEN METABOLISM
OF THE BRAIN, ITS ELECTRICAL ACTIVITY AND THE CONDITIONED
REFLEX ACTIVITY OF ANIMALS AFTER VIBRATION

L. D. Luk'yanova, A. V. Kol'tsova, Ye. S. Meyzerov
and Ye. P. Kazanskaya

ABSTRACT

Rats were exposed to whole-body vertical vibration (7C cps, 0.4 mm, 15 min) six times a week (total of 30). It was found that the changes in different indices of the functional state of the CNS have a phase character. A study was made of oxygen consumption in cerebral tissues, total bioelectric activity, very slow oscillations and conditioned reflex activity.

The first period (1st-4th vibrations) was characterized by the appearance of postvibration generalized inhibition in the higher parts of the brain. In the second period (after the 4th vibration) a compensatory-adaptative process developed, contributing to relative normalization of functions. The third period (after the 20th-25th vibrations) was characterized by a total decrease in the functional activity of higher parts of the CNS.

Investigations made for the purpose of studying changes occurring during and after stimulation by vibration have revealed the presence of a definite phase character in the course of oxidation processes of the brain (Luk'yanova, 1964). It was of interest to compare these data with a number of other indices of the functional activity of the higher parts of the CNS. /105

For this purpose we undertook a study, using these same animals with multiple (up to 30) exposures to vibration, of the level of oxygen consumption in different parts of the brain and the patterns of change in electrical activity. Presently available investigations of the EEG after vibration apply for the most part to cases with already clear manifestations of vibration sickness, and they shed virtually no light on the initial stages of this sickness and its latent period (Shpil'berg, 1962, 1964; Ginzburg, 1964, and others). There is a complete lack of systematic investigation of the electrical activity of the brain from the beginning of application of a vibration stimulus.

In this study, in addition to an analysis of changes in the background electrogram, we have analyzed changes of very slow fluctuations in potential, characterized by a period of 0.5-0.8/sec and an amplitude of 0.3-1.5 mV (Aladzhalova, 1956; Aladzhalova, Koshtoyants, 1957, 1960), and hourly oscillations of electrical activity, representing a periodic change in the level of activity in the electrogram, occurring over a period of several minutes (Aladzhalova, Kol'tsova, 1962, 1963a,b). We further analyzed a burstlike form of activity in the electrogram, expressed in the periodic appearance of groups of waves, against the background of the electrogram characterized by great regularity and large amplitude and different from the background in frequency (Aladzhalova, Kol'tsova, 1963a,b, 1964a).

Rapid and very slow electrical activity and measurement of the magnitude of the current characterizing oxygen tension in the tissues were recorded alternately with the same bipolar electrodes (L. D. Luk'yanova and Ye. P. Kazanskaya, p. 85). Leads were from the sensorimotor, auditory and visual regions of the cortex of the large hemispheres and from the motor zone of the subcortex (caudate nucleus). At the time of the experiment the animal was free within the chamber.

The very slow oscillations of potential were recorded by a dc amplifier with symmetrical input (Aladzhalova, 1956) and with an output to an N-373/2 loop oscillograph with a sensitivity of 10^{-6} A.

More rapid activity was recorded with a low-frequency 4-channel EEG-1M amplifier with pen recording.

Change in Brain Oxygen Metabolism Associated With Multiple Vibration

In our previously published study (Luk'yanova, 1964) we noted that even ten exposures to vibration led to the appearance of an increase in the duration of the phase of increase of oxygen consumption arising in the course of vibration stimulus. After vibration a phase of decreased consumption was observed in the animals, compared to the normal consumption of oxygen by the cerebral tissues. This state, appearing very rapidly during the first exposures to vibration, developed after the tenth vibration at a somewhat later time, due to lengthening of the excitation phase.

The use of a large number of vibrations (to 30) made it possible for us to conclude that the lengthening of the phase of increased oxygen consumption can lead to the virtual disappearance of the first inhibition phase; the second wave of decrease in oxygen consumption, setting in 1-1.5 hr after the end of vibration, apparently corresponds to internal rather than protective inhibition. In the experimental animals a stable increase in oxygen metabolism was

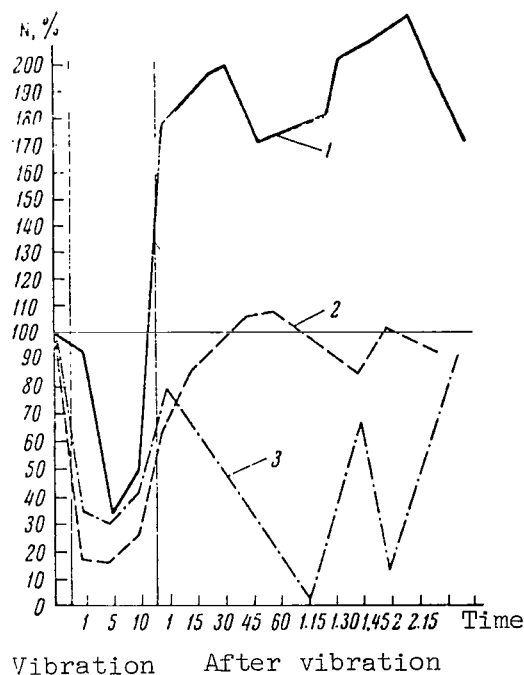


Figure 1. Change of ΔI_{\max} in visual region of cortex, expressed in percent of norm, during and after first (1), fifth (2) and 25th (3) exposures to vibration. Decrease in ΔI_{\max} is evidence of increase in oxygen consumption, whereas increase of ΔI_{\max} indicates decreased oxygen consumption in the investigated region.

maintained so long that successively arising inhibition did not appear at all. A stationary increase of cerebral metabolism was observed in all investigated parts and progressed with an increase in the number of vibrations¹ (fig. 1).

¹The decrease in oxygen consumption was judged from an increase in ΔI_{\max} , and the increase of oxygen consumption was judged from a decrease in ΔI_{\max} . For a detailed explanation see the articles of L. D. Luk'yanova (1964b) and L. D. Luk'yanova and Ye. P. Kazanskaya, p. 85.

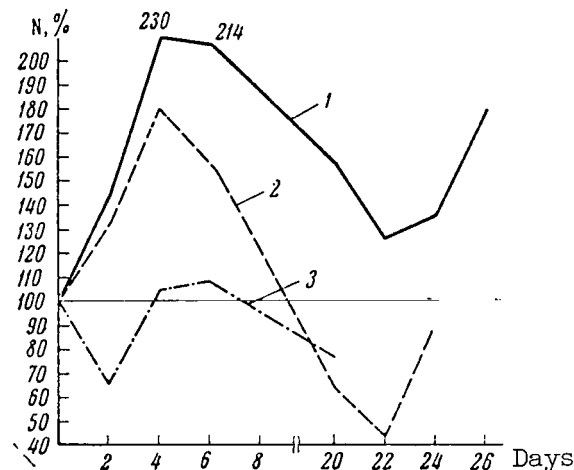


Figure 2. Changes in background ΔI_{\max}

on different days in the case of daily and multiple exposure to vibration. See fig. 1 for an explanation of the character of changes.

1, Sensorimotor region of cortex;
2, visual region of cortex; 3, motor region of cortex.

An investigation of changes in background oxygen consumption on different days also revealed definite changes apparently related to trace phenomena /108 persisting a long time after vibration.

For example, in the sensorimotor and auditory regions of the cortex we observed a decrease in background oxygen metabolism up to the fifth vibration followed by a period of relative normalization in the sensorimotor region of the cortex and an increase in background oxygen consumption in the auditory cortex. Finally, there was a period of a secondary decrease in oxygen metabolism (fig. 2).

In the subcortical region there also was a definite phase character in the change of background oxygen consumption. The oxygen tension in all investigated regions for all animals remained virtually unchanged. The scatter of ΔI_{\max}

values in the background increased with an increase in vibration exposure (table 1)

TABLE 1. CHANGE OF SOME PARAMETERS CHARACTERIZING BACKGROUND CONSUMPTION OF OXYGEN IN BRAIN TISSUES OF SENSORIMOTOR CORTEX IN RAT NO. 10 AS RESULT OF MULTIPLE VIBRATION.

Date	No. of measurements	h_{mean} (cm)	$S_{\Delta I}$ (cm ²)	h_{max} (10 ⁻⁴ A)
6.I 1965	1	0,64	5,76	0,090
	2	0,81	7,30	0,065
	3	0,70	6,26	0,055
	4	0,70	6,26	0,053
	5	0,74	6,17	0,065
After 16th vibration				
26.I 1965	1	0,55	5,02	0,058
	2	0,81	7,30	0,070
	3	1,11	10,00	0,094
	4	1,20	10,70	0,068
	5	0,80	8,11	0,068

NOTE: Commas in tables represent decimal points.

Change in Very Slow Fluctuations of Cerebral Potential in Rats After Vibration

The parameters of very slow fluctuations of the potential recorded in rats were similar to those described for rabbits and man (Aladzhalova, 1962). Second-long rhythms with a frequency of 6-11 oscillations/min and an amplitude of 0.3-1 mV and minute-long rhythms with a frequency of 1-1.5 oscillations/min and an amplitude of oscillation of 0.5-1 mV were observed. /109

The investigation of very slow oscillations of the potential in the period when the animal was being acclimatized to the experimental conditions (without exposure to vibration) revealed that on the second and third experimental days there was considerable intensification relative to both frequency and amplitude (by a factor of 2-3). By the fourth experimental day the very slow oscillations were restored to the initial value (fig. 3). This apparently is related to the development and extinction of the orienting reflex.

Fifteen-minute vibration led to definite subsequent changes in very slow fluctuation of the potential, which were manifested in the form of two stages of intensification at times of 5-30 min and 60-160 min respectively (fig. 4). The changes of very slow fluctuations of the potential were observed even after a 5 min vibration, and they intensified during repeated (after 1-1.5 hr) exposures to vibration. Thus, in this case there apparently was a summation of vibration stimuli, intensifying very slow fluctuations of the potential. The

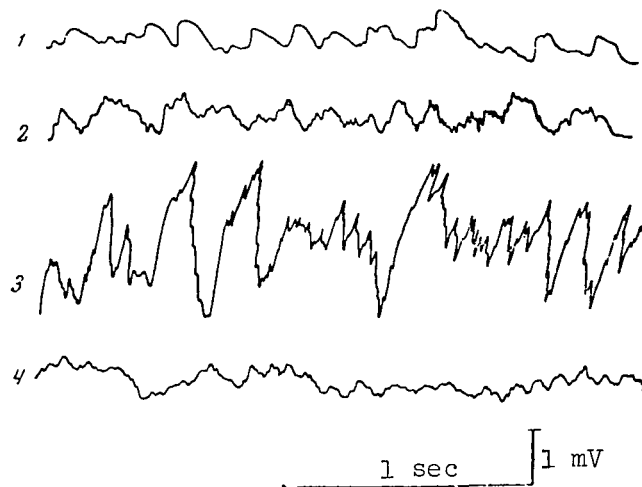


Figure 3. Change of very slow fluctuations of the potential in the auditory region of the cerebral cortex during acclimatization to experimental conditions.

1, First experimental day; 2, second; 3, third; 4, fourth experimental day.

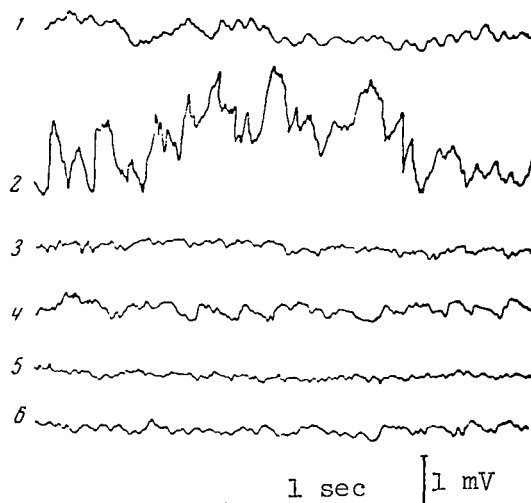


Figure 4. Change of very slow fluctuations of the potential in the auditory region of the cerebral cortex after the first exposure to vibration stimulus for period of 15 min.

1, Background (before vibration); 2, 25 min; 3, 37 min; 4, 65 min; 5, 115 min; 6, 145 min after exposure to vibration.

restoration of the background of very slow fluctuations after vibration /110 occurred in 2.5-3 hr, but not in all experiments. Return to normalcy was not observed in several cases even after 3.5 hr. However, on the first days of application of vibration, the background of very slow potential fluctuations was restored after 24 hours.

Later, with an increase in the number of exposures to vibration (not less than 15) there was a sharp and apparently prolonged or irreversible decrease of very slow fluctuations in amplitude. The stability of this state is confirmed by the fact that a cessation of vibration for several days did not lead to restoration of very slow oscillations.

Change of Hourly Oscillations of Electrical Activity,
General Form of Cerebral Electrogram and Burst
Activity of Rats After Vibration

Hour oscillations of electrical activity were observed at the norm in all investigated structures of the brain. Each wave of hour oscillations (increase of amplitude in the EEG) fell either against the background of persistence of the former frequency (in most cases), or its decrease (fig. 5). Later we /111 made an analysis of the level of activity only in amplitude. The simultaneous records of the electrogram from different structures revealed that the waves of hour oscillations appeared synchronously in all or some of the recorded regions, and asynchronously as well.

Upon adaptation to the experimental conditions, the latent period of appearance of hour oscillations of electrical activity had a tendency to increase. The number of waves of oscillations in this case decreased, and each wave became increasingly elongated. This phenomenon, noted in other animals by N. A. Aladzhalova and A. V. Kol'tsova (1962, 1963a,b), apparently is a reflection of a general biological law formulated by P. I. Gulyayev (1956). According to his findings, at the stimulation threshold, with a gradual transition into a state of specific activity, all excited systems first develop an unstable fluctuating activity, and only then does a stable and regular activity become established.

In the period of vibration, as demonstrated earlier (L. D. Luk'yanova and Ye. P. Kazanskaya, p. 75), the electrical pattern in the investigated regions differs so sharply from the norm, that it was not possible to analyze the /112 changes of the hour oscillations in this period.

However, in the postvibration period it was possible to define three periods associated with clear changes of the hour oscillations of electrical activity.

The first period (first several vibrations) was characterized by the fact that even 5-15 min later there was a clearly expressed intensification of the expression of hour oscillations of electrical activity (increase of number of oscillation waves and amplitude of oscillations).

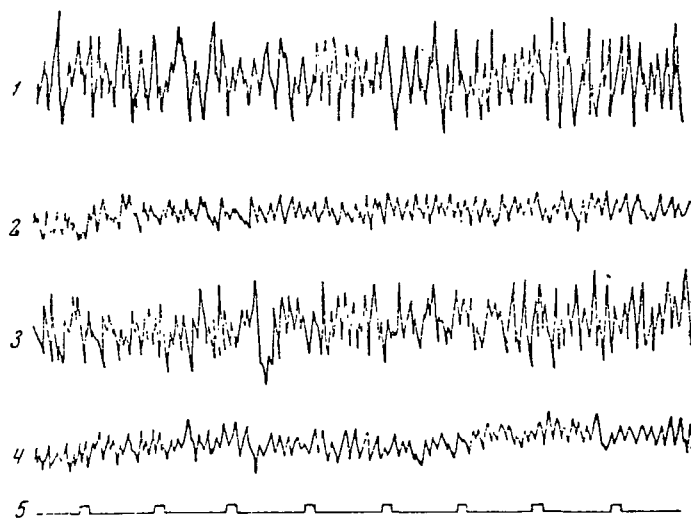


Figure 5. Example of hour oscillations of electrical activity in sensorimotor region of cortex in rat No. 17.
1, 2, 3, 4, Different times in same experiment;
5, time reading in sec.

The second period, setting in after 4-6 vibrations, was characterized by a decrease in the number of waves of hour oscillations, with a simultaneous increase of the specific weight of activity with a great amplitude, that is, there was the same pattern of change of hour oscillations of electrical activity observed during habituation of the animal to the experimental conditions. However, this occurred against the background of a general decrease of the amplitude level of electrical fluctuations.

The third period, appearing after the 25th vibration, again was characterized by an increase in the number of waves of hour oscillations. This period continued without significant changes up to the end of the investigations.

Against the background of development of hour oscillations of electrical activity there appeared a burstlike form of activity. The bursts occurred both at the high-amplitude level of activity and at the low-amplitude level and were observed in all investigated structures. They could appear both synchronously, in generalized form, and locally in only some of the recorded structures (fig. 6).

Upon adaptation to experimental conditions, there was a gradual decrease in the burstlike activity of the motor and visual regions and of the subcortex. In the auditory region there were no decreases in the burstlike activity, which possibly was related in this case to greater activation of the auditory analyzer in animals sitting motionless in the chamber. After the first exposures to vibration, there was an intensification of the burstlike activity.

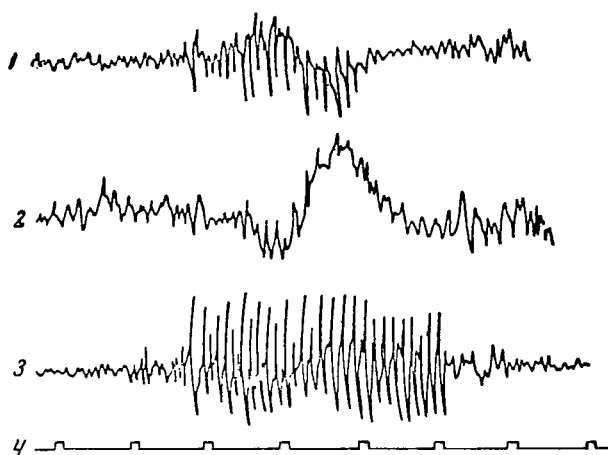


Figure 6. Example of burstlike activity in brain structures of the rat.
1, Sensorimotor region of cortex; 2, visual region of cortex; 3, caudate nucleus; 4, time reading in sec.

There was an increase of the number of bursts and their density, that is, the number of bursts per unit time. The maximum number of bursts occurred at the time of the 3d-6th vibrations. Later, with an increase in the number of vibrations, there was a decrease of the burstlike activity, more clearly expressed in the auditory region. This process developed in wavelike fashion, up to complete disappearance of bursts after the 26th vibration.

A more detailed analysis of the electrogram for animals subjected to multiple vibration also revealed three main periods in development of the after-effect reaction.

The first period (4th-8th vibration) was characterized by the fact /113 that with cessation of the effect of exposure to vibration, the high-amplitude hypersynchronized sinusoidal rhythm, setting in at the time of vibration, as demonstrated in the article of L. D. Luk'yanova and Ye. P. Kazanskaya, p. 75, persisted for some time (30-60 sec). Then, after a short phase of desynchronization, there was a clearly expressed manifestation of a burstlike activity. This activity was expressed better in the caudate nucleus, to a somewhat lesser degree in the sensorimotor cortex, and could not be detected at all in the visual region of the cortex. Figure 6 shows the propagation of such a burst from the motor region of the subcortex into the sensorimotor cortex. The predominance of the burstlike activity in the first 30 min after exposure to vibration coincided in time with the appearance of a decreased oxygen consumption in these same animals and the complete extinction (as we will see below) of conditioned and unconditioned reactions. It can be assumed, therefore, that intensification of the bursts at this stage reflected a state of inhibition, developing in the higher parts of the CNS (fig. 7).

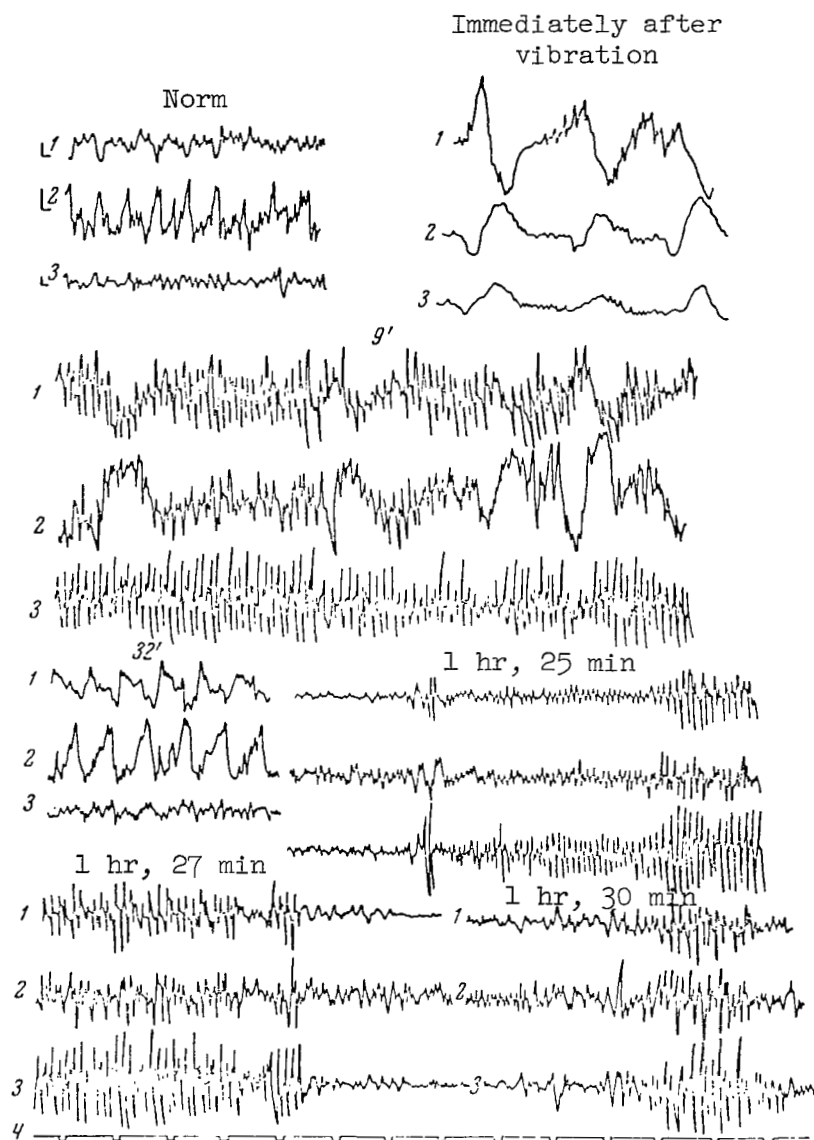


Figure 7. Change of rapid electrical activity after 4th vibration (first period) in rat No. 17. Minutes and hours indicate time elapsing after vibration. Other notations same as in fig. 6.

Thirty-sixty minutes after vibration in the cortex and sometimes the subcortex as well we observed the appearance of slow synchronous rhythms /115 of the delta wave type with a frequency of 2-3 cps usually appearing during sleep. Since this period coincided with a secondary decrease in oxygen consumption in the cerebral tissues after vibration, such a picture can apparently be related to the appearance of a second wave of diffused inhibition transpiring in a similar manner to internal inhibition. On the first days after

exposure to vibration, this period lasted several tens of minutes; later it was reduced in time (to 1 min). Upon completion of this period there was depression of rhythms in all investigated parts of the brain, periodically alternating with a high-amplitude burstlike activity. Restoration of electrical activity to the initial values observed prior to vibration could not be recorded in any investigated part of the brain, even 3 hr after exposure.

The second period of changes of bioelectric activity of the brain during a regularly repeated exposure to vibration was characterized primarily by a change in background activity.

Whereas prior to exposure to vibration during the investigation of the animal's electrogram we could define several basic, typical forms of rapid fluctuations, in the second period the electrical activity of the brain was characterized by extraordinary instability, the appearance of individual high-amplitude slow oscillations (1 cps and more) and intensification of the burstlike activity (increase in both density of the bursts and duration of their appearance). After vibration stimulation there was a depression of rhythms, persisting a long time in all investigated regions. In this period there was no restoration of background activity to the initial previbration level for a period of several hours after exposure, and depression predominated 1-1.5 hr after vibration.

The third period, occurring after the 20th-25th vibration, was characterized by disappearance in the background activity of a broad range of rhythmic oscillations, observed earlier, especially in the second period, with decrease of the amplitude of activity to complete depression of the rhythms. The burstlike activity in the animals prior to vibration disappeared. After vibration we observed prolonged (to 10 min) persistence of synchronized high-amplitude sinusoidal oscillations, manifesting (as mentioned in the article by L. D. Luk'yanova and Ye. P. Kazanskaya) again in this period, at the time of the vibration itself, their still greater infrequency and increased amplitude. Then alternate rhythms appeared, either with periods of complete depression or with low-amplitude synchronized oscillations with a frequency of 7-8/sec.

If slow oscillations did not appear at the time of vibration, immediately following it were periods of complete depression of rhythms, alternating with low-amplitude synchronized oscillations with a frequency of 8 cps (fig. 8). /116

The picture of changes in electrical activity at different levels of the brain described here is an extreme case, and characterizes the development of a reaction in animals which apparently are exceedingly sensitive to vibration. In cases when this reaction was less clear and when in the course of vibration there were no hypersynchronized sinusoidal oscillations, there nevertheless was a clearly expressed decrease in the frequency of oscillations in the after-effect, with persistence or slight increase in their amplitude. This process was expressed with identical clarity in the different parts of the cortex and coincided in time with the first and second decreases in oxygen consumption in these same parts of the brain.

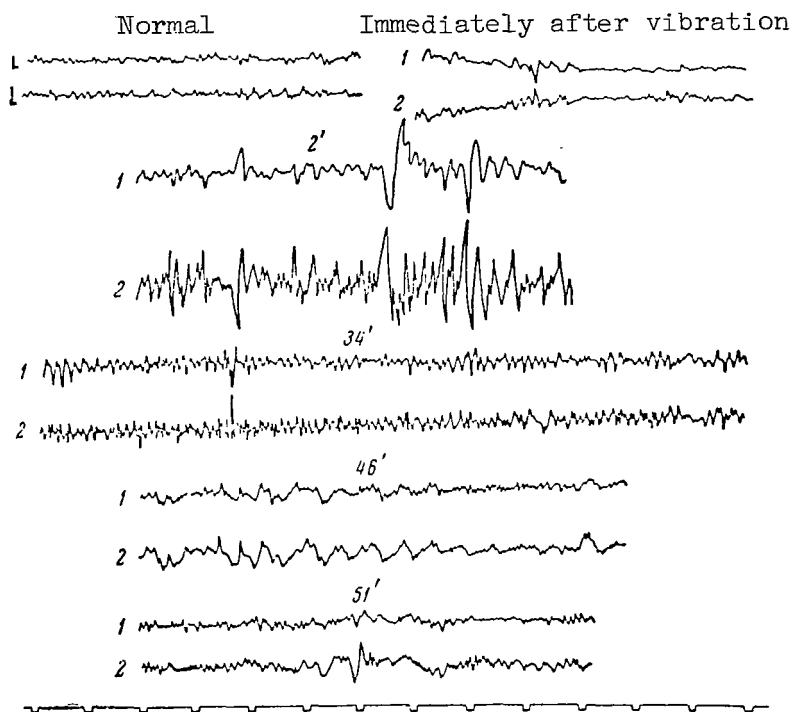


Figure 8. Change of rapid electrical activity during the 3rd period in rat No. 17. Notations same as in fig. 6.

The Effect of Multiple Vibrations on the Conditioned Reflex Activity of Animals

The literature on this problem and the research methods are presented /117 in the article by N. N. Livshits and Ye. S. Meyzerov, p. 61.

The animal was exposed to 27 daily vibrations (except Sundays). Experiments were carried out immediately after each vibration and three hours later. Normally the animal was characterized by stable conditioned reflexes (fig. 9), proper force relationships and absolute differentiations. From time to time there were inter-signal reactions.

Adjustment of the electrodes did not cause any appreciable deviations of higher nervous activity from normal.

After the first vibration, the artificial and natural conditioned reflexes were completely absent (fig. 9) and the motor activity of the rat was inhibited. During the entire time of the experiment the animal was in a state of deep internal inhibition.

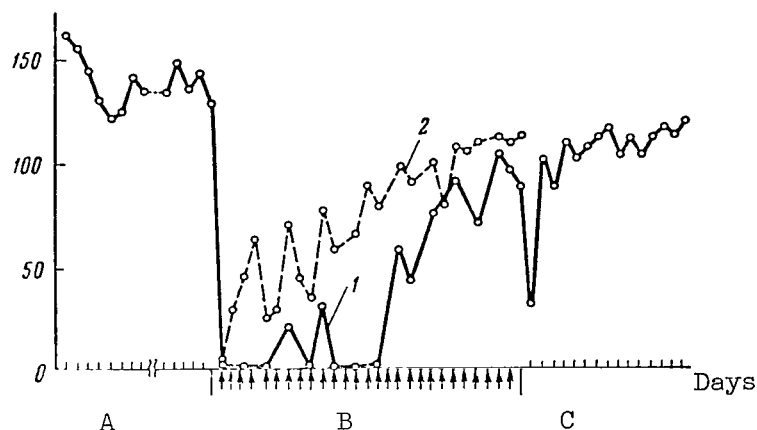


Figure 9. Effect of multiple vibrations on the mean total value of conditioned reflexes. Along x-axis -- time in days. A, Normal; B, period of vibrations; C, after cessation of vibrations. Along y-axis -- mean total values of conditioned reflexes in relative units. 1, Immediately after vibration; 2, 3 hr after vibration.

Subsequent vibrations also caused serious disruptions of conditioned reflex activity, expressed by complete extinction of artificial conditioned and part of the natural conditioned reflexes. The experiments made three hours after the first four vibrations revealed deep disruptions of higher 118 nervous activity, similar to the phenomena observed in experiments carried out immediately after vibrations. On the day of the first exposure there was no difference in the conditioned reflex activity of a rat in examinations carried out immediately after vibration and three hours later. Beginning with the 10th vibration there was some improvement of higher nervous activity, compared to the preceding period. At this time artificial conditioned reflexes usually were absent only in the second half of the experiment, but, the latent periods of the reflexes present were considerably lengthened, compared to the initial background (fig. 10). In individual cases there was refusal to take food. The higher nervous activity of the rat remained at this level with insignificant fluctuations until the 21st vibration. In the experiments carried out three hours after the vibrations, there was partial restoration of conditioned reflex activity according to a number of indices. After the 21st vibration, despite continuing exposure, there was further improvement of higher nervous activity.

In this period there were no extinctions of artificial conditioned reflexes for either strong or weak stimuli, but the values of the reflexes remained considerably below the initial values (fig. 9). The latent periods became shorter, but did not reach the norm. We observed this same picture after further exposures to vibration and in the course of four days after their cessation.

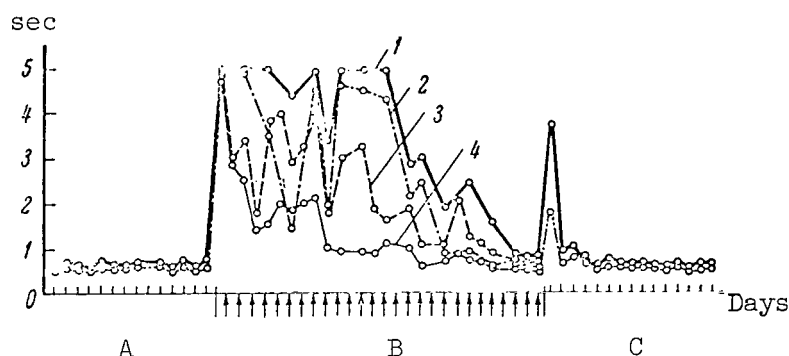


Figure 10. Effect of multiple vibrations on mean latent periods of formed (artificial) conditioned and natural reflexes.

Along x-axis -- time in days. A, Normal; B, period of vibrations; C, after cessation of vibrations. 1, 2, Immediately after vibration; 3, 4, 3 hr after vibration; 1, 3, formed (artificial) conditioned reflexes; 2, 4, natural conditioned reflexes.

In the experiments carried out three hours after vibrations there was ¹¹⁹ some improvement of the higher nervous activity of the rat, as compared to its state immediately after vibrations on the same day of this period (figs. 9 and 10). However, in not one of the experiments, carried out even three hours after vibration, did the state of the higher nervous activity of the rat approach its initial level. Observations were continued for 23 days after the end of vibrations. Prior to the end of observations the higher nervous activity of the rat still had not returned to its initial level. However, in this period there was an obvious tendency to its normalization. There were response reactions to all positive stimuli, but their values were lower than at the normal (fig. 9); the latent periods of both artificial and natural conditioned reflexes decreased still more and reached the initial level (fig. 10). There were no rejections of food during this period. In not one of the experiments carried out in the postvibration period were any phase phenomena discovered.

It should be noted that in all the experiments, without exception, which were carried out both in the period of vibrations and after their cessation, the differentiated inhibition of the rat was stable, and a test with lengthening of differentiation to 60 sec, carried out on the 5th day after cessation of vibrations, did not cause its disruption.

Discussion of Results

Comparison of the changes of the functional state of the higher parts of the brain, investigated in this study by various methods, indicated definite

patterns of their development in the case of multiple, repeated exposure to vibration and differentiated them from the possible changes observed in normal animals.

In particular, there is a completely definite phase character in the changes of different indices of the functional state of the CNS in response to exposure to vibration. The time parameters of the most clearly expressed changes for each investigated index agree well with one another.

For example, in all cases we succeeded in defining the first period in the response reaction of the animal to vibration. Judging from the changes in oxygen consumption, it was expressed in a sharp decrease in oxygen metabolism in cerebral tissues after vibration, which could be an expression of the appearance of a state of generalized inhibition in the higher parts of the brain. This opinion is confirmed by experiments on investigation of the conditioned reflexes in animals after vibration, in which it was demonstrated that there was complete extinction in the course of several hours after exposure (first four vibrations). This picture is evidence of a sharply expressed attenuation of the excitation process in the nervous system, expressed in the extreme phase of protective inhibition. The absence of disinhibition of differentiations in this period apparently indicates a summation of the protective and natural inhibitions. The picture of the electrical activity of the brain in this period also is confirmation of the concept of the presence of a long persisting state of inhibition in the investigated regions of the brain, arising in place of overexcitation of the nerve centers during vibration (L. D. Luk'yanova and Ye. P. Kazanskaya). /120

The complete coincidence of the two phases of intensification of very slow potential with time with a decrease in oxygen consumption of the cerebral tissues in this period is a weighty demonstration of the interrelationship between this type of electrical activity and the oxygen metabolism of the brain. It should be noted that N. A. Aladzhhalova (1962) in her study also demonstrated an intensification of the very slow fluctuation of potential after prolonged asphyxia.

Therefore, it must be surmised that oxygen metabolism in the tissues is related directly to the genesis of very slow potential. According to available data in the literature (Aladzhhalova, Kol'tsova, 1958), intensification of very slow fluctuations of potential usually is observed under the influence of stress stimuli and under conditions when the effect of some factor becomes systematic. The intensification of very slow oscillations, even 20 min after the first stimulation by vibration, is evidence that in this case there is development of a stressed state. Vibration as a stress stimulus apparently causes serious changes in the different autonomic functions of the body, especially in the neurohumoral interrelations. This, in turn, inevitably should lead to development of instability of nervous processes.

According to the data of N. A. Aladzhhalova and A. V. Kol'tsova (1962) and other authors, the development of unstable states in the nervous system leads to appearance of an oscillatory process in the development of electrical phenomena. Therefore, the intensification of very slow potential fluctuations,

hour oscillations and burstlike forms of activity, which we observed after application of the first vibration and which intensified in the subsequent vibrations (4th-6th exposures), indicates, apparently, that there is a sharp disruption of normal functional interrelations in the nervous system in this period, as a result of which in the continuing stress effect there should be an inevitable subsequent transition of the entire system to a new functional level.

The second period, whose onset in individual cases already could be observed after the 4th vibration, apparently is characterized as a period of /121 appearance of compensatory-adaptative reactions and relative normalization of the functions. This period can be of different duration in different animals, and it occasionally does not appear at all. In those cases when it does develop, it is possible to note a decrease in the changes of oxygen metabolism and some stabilization and normalization of it in the background after a vibration stimulus, appearance of natural, and then artificial conditioned reflexes, at first three hours after vibration, and then at an earlier time, a decrease of burstlike activity on the EEG.

Relative acclimatization to vibration with respect to the pattern of electrical activity, apparently is also reflected in the fact that after stimulation by vibration the total number of oscillations decreases, with simultaneous increase of activity with a high amplitude and decrease of the gap between activity with high and low amplitude. A similar phenomenon is also observed normally during acclimatization to experimental conditions.

However, despite the unquestionable presence of compensatory-adaptative effects and their clear manifestation at the beginning of this period, with an increase in the number of exposures to vibration there is further change of the total functional level. The latter is indicated by a gradual change of background activity of electrical oscillations in animals characterized by exceptional instability, variety of the rhythms, appearance of slow potential fluctuations and intensification of the number and density of bursts. This is also indicated by instability of the background consumption of oxygen in this period, and also by the fact that there is no significant decrease or total disappearance of the hour fluctuations of electrical activity.

Obviously, the observed functional changes stably change the absolute level of constant potential (Rusinov, 1947, 1962) to such an extent that very slow potential fluctuations are not recorded against the background of these changes. As a result, there is a gradual decrease in the amplitude of the very slow fluctuations, until they disappear completely. The electrical activity of the brain of the animal during (L. D. Luk'yanova and Ye. P. Kazanskaya) and after vibration is characterized in this period by a gradual replacement of all observed rhythms by their depression.

The third period (after the 20th-22nd vibrations) is characterized by an increase of oxygen consumption during vibration which is more clearly expressed but it is not replaced later by a phase of depression of oxidation processes. This fact forces us to assume that protective inhibition does not develop at

this stage after stimulation by vibration. The state of conditioned reflex activity in this period completely confirms this opinion. As we have seen, specifically at these times (after the 21st vibration) there was a clearly expressed tendency to restoration of conditioned reflex activity. There was a considerable decrease in the value of the latent periods and an increase /122 in the intensity of the reflex, although both these indices failed to return to the initial level. The earlier observed frequent cases of extinction of artificial and natural conditioned reflexes did not occur at all; the force relationships were correct.

However, analysis of the EEG revealed that this relative normalization was accompanied by a gradual change in electrical activity. In particular, the most characteristic feature was the appearance of a depression of rhythms during and after vibration and its predominance in the background activity of the EEG in different parts of the brain, and especially in the cortical regions. In this same period there again was a tendency toward decreased background oxygen consumption by the cerebral tissues. There was an increase in the number of cases when in response to stimulation by vibration there was no typical picture with the appearance of slow hypersynchronized oscillations (L. D. Luk'yanova and Ye. P. Kazanskaya, p. 75), and the EEG maintained a flattened appearance, almost without any rhythms. These observations indicate a decrease in the excitability of the cortex to spontaneous peripheral impulsion or a partial blocking of the latter at the subcortical level. The appearance of minor synchronization, occurring in individual cases in this period after vibration at a very low amplitude level, apparently is also an expression of the involvement of nerve cells, whose excitability is greatly decreased. Therefore, the partial improvement of conditioned reflex activity is not an indication of normalization of the functional state of the cortex, but indicates that due to a decrease in excitability the cortex no longer reacts to vibration in the way observed in the first exposures to vibration.

This also is indicated by the fact that the conditioned reflexes remain at a low level for three weeks after cessation of vibration. Such a decrease of excitability is of adaptative significance protecting the cortex against extreme stimulation.

From this point of view we can also understand the picture of altered oxygen consumption in individual animals, when there is progressive increase of the phase of its increased utilization, up to complete disappearance of the state of decreased oxygen consumption by cerebral tissues, developing at the time of the first exposures to vibration. Against the background of a general decrease of excitability to peripheral impulsion, the vibration stimulus can no longer cause overexcitation of neural elements, and protective inhibition also does not appear. Thus, lengthening of the phase of increased oxygen consumption expresses only a relative, minor, and brief functional revitalization of the operation of the brain against a background of a general stable depression of its metabolism, and it is not related to a transition /123 of the body to a new, higher functional level.

A similar external manifestation, expressed in a decrease of the inhibition phase after vibration, although having a different mechanism, was observed

in our investigations after an artificial decrease of the flux of peripheral impulsation as a result of a partial surgical destruction of the auditory apparatus (L. D. Luk'yanova and S. M. Ambrosova, p. 88). The disappearance of the burstlike activity is apparently also related to a decrease in the excitability of the higher parts of the brain.

Thus, summarizing the above, the general conclusion may be drawn that as a result of systematically repeated exposure to stimulation by vibration the animal body is subjected to a long functional reorganization of its activity. However, due to the extreme character of the investigated stimulus, causing disequilibrium of the most vitally important system -- the higher parts of the brain -- and leaving a prolonged aftereffect in them, capable of summation, the compensatory mechanisms are inadequate for restoring and maintaining a normal or near-normal functional level. As a result, there is gradual exhaustion of nervous processes, leading to a general decrease in general functional activity.

The wavelike development and rate of onset of vibration sickness apparently depend on the intensity relations between inhibition and excitation processes. In the case of exceptionally strong excitation and inhibition processes and the presence of highly developed compensatory adaptations, there can be a considerably longer resistance of the body to vibration, in other words, persistence of a quite high level of functional activity of the body. However, in the cases analyzed in this study there was a progressive decrease in the functional level, against whose background the response reaction of the different investigated indices decreased during exposure to vibration. From the point of view of protection of the body, this may also be considered a forced compensatory-adaptative effect, occurring at a low level, and while not stable, nevertheless to some degree protects the brain from exceedingly rapid exhaustion of the nerve cells from systematic overexcitation.

Conclusions

1. Systematic multiple application of a vibration stimulus (frequency 70 cps, amplitude 0.4 mm, exposure time 15 min) causes phase changes in different indices of the functional state of the CNS in rats (oxygen consumption by 124 cerebral tissues, very slow potential fluctuations, hourly oscillations, burstlike activity, general electrical activity of the brain, conditioned reflex activity of the animals).

2. The first period of changes as a result of the effect of vibration (1st-4th exposures) is characterized by the development in the higher parts of the brain of a poststimulation state of generalized inhibition (decreased oxygen consumption by the brain tissues, corresponding changes in the EEG, intensification of very slow potential fluctuations, total extinction of conditioned reflexes).

3. The second period (after the 4th vibration) is related to the development of compensatory-adaptative processes and relative functional normalization

(decrease of changes in oxygen consumption by cerebral tissues, decreased burst-like activity in the EEG, appearance of natural and then artificial conditioned reflexes).

4. The third period (after the 20th-25th vibrations) is characterized by a general decrease in the functional activity of higher parts of the brain (decreased background consumption of oxygen, depression of background electrical activity during and after vibration, and a decreased level of conditioned reflex activity for a long period after exposure to the last vibration).

RESPIRATORY CHANGE DURING VIBRATION

Ye. P. Kazanskaya and L. D. Luk'yanova

ABSTRACT

Rats were exposed to whole-body vertical vibration (frequency 70 cps, amplitude 0.4 mm, exposure time 15 min). External respiration during vibration was investigated.

It was found that in the first half of the vibration time there was increase in respiration frequency. No general tendency in responsive reaction could be detected in the second half of the vibration period or in the post-vibration period. It is concluded that the changes in oxygen metabolism induced by vibration are not related to respiratory changes.

It is insufficient to study any one function when investigating the /125 influence of vibration on the human or animal body.

Since changes in oxygen metabolism may be related to disruption in its supply to the brain tissues, caused by corresponding changes in both the cardiovascular and respiratory systems, the purpose of this study was to explain the changes in external respiration in response to a vibration stimulus.

The references in the literature to this problem (Chü Chung-hsiang, 1957; Lebedeva and Chü Chung-hsiang, 1958) pertain to the effect of low-frequency vibrations (3-25 cps). In these studies the authors mention acceleration of respiration and increase of its intensity in the first 5-8 min of vibration. After eight minutes the character of the reaction changed in the direction of slowing of respiration. The same picture was observed after vibration.

It was of interest to compare the changes occurring in the higher parts of the CNS, during a 15 min period of vibration with a frequency of oscillations of 70 cps and an amplitude of 0.4 mm, with the changes of respiration observed during a period of vibration of these same parameters.

The work was done with male rats of the Wistar line weighing 200-250 g. Respiration was recorded with a special sensor attached to the chest of the rat and with a EKPSch-3 electrocardiograph.

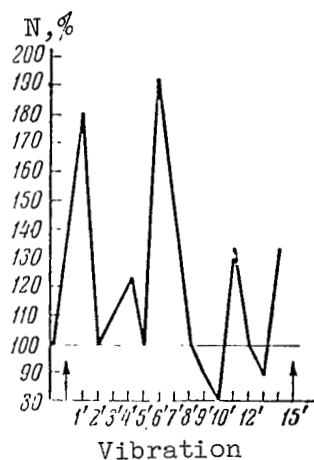


Figure 1. Change in the wave of respiratory movements during exposure to vibration.

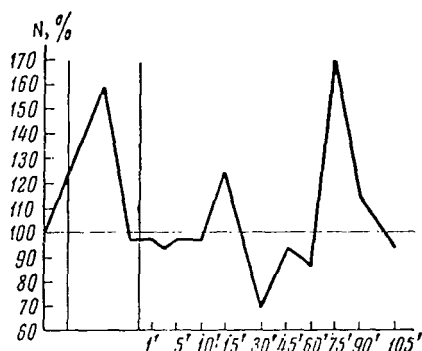
Along x-axis -- time from onset of exposure to vibration, in min. Along y-axis -- frequency of respiratory movements, expressed in percent of mean initial level.

Figure 1 shows in detail the changes in respiration during the time of vibration for rat No. 6. The figure shows that respiration was characterized by extreme irregularity. Its frequency increased sharply at the first moment of vibration, and to the very end it was characterized by an alternation of large and sharp rises with similar fluctuations to and below normal.

Figures 2 and 3 show a more general picture of respiration during the 126 time of vibration and during the postvibration period. We see that in the first period of vibration there was a general tendency to an increase in respiratory frequency. In the second half of the vibration period and in the postvibration period the reaction was manifested differently in different rats.

The change of respiration in rat No. 1 is shown in figure 2. The illustration shows that in the second period of exposure to vibration there was a decrease in respiration frequency, and in the first 10 minutes after vibration there was an almost complete normalization of respiration. During the subsequent period of observation after vibration the respiration had a fluctuating character and had two maxima of excitation.

Figure 3 shows the change of respiration in rat No. 3. Here we observe a different picture than in figure 2. At the beginning of the second period of exposure to vibration the respiration frequency decreased, but at the very end it increased sharply and was maintained at this high level for 15 min after vibration. Beginning with 15 min, the respiration was characterized by irregularity, and the curve reflecting its frequency varied about a mean level with greater or lesser variations.



Vibration After vibration

Figure 2. Changes in the wave of respiratory movements during and after exposure to vibration. Notations same as in fig. 1.

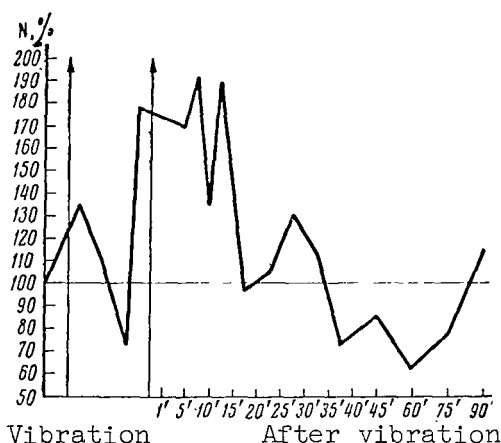


Figure 3. Changes in the wave of respiratory movements during and after exposure to vibration (rat. No. 3). Notations same as in fig. 1.

It therefore may be concluded that in the first half of the period /127 of exposure to vibration there was an increase in respiration wave in all cases. In the second half of vibration and in the postvibration period it was not possible to detect a general tendency in the response.

In earlier studies by one of the authors (Luk'yanova, 1964) it was demonstrated that oxygen metabolism under the influence of vibration changes sharply and has a two-phase character. During vibration the oxygen consumption increases and has a wavelike character after vibration. Therefore, it was

interesting to determine whether there is a relationship between changes in oxygen metabolism and changes in external respiration during exposure to vibration.

In comparing the results of this study with data obtained in an investigation of oxygen metabolism it can be noted that in the first period of vibration there is a parallelism between changes occurring in oxygen metabolism and changes in the respiratory system, that is, the animal experiences a phase of increased stimulation. However, such a parallelism is not observed subsequently. This indicates that changes in oxygen metabolism occurring under the influence of vibration are unrelated to changes in respiration.

EFFECT OF ACUTE X-IRRADIATION ON VENOUS CIRCULATION
IN THE CEREBRAL VESSELS OF A RABBIT

V. Ya. Klimovitskiy

ABSTRACT

Cerebral venous blood flow was measured using thermistors for study of the cerebral surface veins of rabbits exposed to X-irradiation. In one group of animals the back and abdomen were irradiated by a dose of 2000 r. Other animals were exposed to total irradiation in a dose of 1000 r.

In both cases a decrease in the level of cerebral blood flow was observed in the irradiated rabbits compared to control during the first hours after irradiation. Locally irradiated animals were observed for 6-8 hours. Whole-body irradiated rabbits survived after exposure and were observed until their death from radiation sickness. In these animals a second decrease of cerebral blood flow was observed 1-2 days prior to death.

The data obtained are discussed in relation to data in the literature concerning the effect of irradiation on general and cerebral hemodynamics.

The purpose of this study was to investigate the rate of circulation /129 in the cerebral veins of rabbits exposed to local or whole-body X-irradiation. Obtaining detailed data on the state of cerebral hemodynamics in irradiated animals is necessary for clarification of the role of vascular disruption in the reactions of the CNS to radiation.

The irradiation doses used are encountered in medical practice only in emergency situations. However, in experiments on animals the mechanism of the effect of acute irradiation in lethal doses continues to be the object of investigation and this applies in particular to the effect of ionizing radiation on the CNS, whose blood supply in radiation reactions has yet been poorly investigated.

The experiment data serving as a basis for this study were obtained in 1958. The recently published investigations of a number of authors in the field of the effect of ionizing radiation on general and cerebral hemodynamics broaden the possibilities of interpretation and generalization of our data.

In our experiments we recorded the volume rate of blood flow in the large surface veins of the brain of a rabbit using pulse-type heat exchange sensors (Klimovitskiy, 1964a,b). R. M. Lyubimova-Gerasimova (1962) used a method similar to ours; she employed M. Ye. Marshak thermoelectrodes which are used for the most part for recording relatively brief reflex changes in blood flow, appearing in response to a particular specific effect. Our sensors were intended for evaluating the level of blood flow in values comparable for the entire period of the experiment on a particular animal and read from a uniform initial level. At the same time, they are not suitable for recording processes with a time constant less than 10 sec.

The experiment was carried out with 45 male rabbits weighing 3.5-4 /130 kg, of which 11 were irradiated locally (part of the back and stomach from the processus spinosus to the pelvic region) in the acute exposure experiment. The irradiation dose was 2000 r. Eleven animals served as a control for this group. The blood flow sensors were attached to 23 rabbits for 5-7 days before irradiation, and blood flow at rest was recorded for these animals for 3-5 days before radiation exposure. Two of them were then exposed to irradiation under the same conditions as the animals of the preceding experimental group. Another 12 rabbits received a whole-body dose of 1000 r, and the remaining 9 served as a control for the latter group.

Irradiation conditions.

- A. 1000 r, 180 kV, 15 mA, filter Cu 0.5, dose intensity 9.25 r/min, skin-focal length 70 cm.
- B. 2000 r, 165 kV, 15 mA, filter Cu 0.5, dose intensity 28 r/min, skin-focal length 40 cm.

During local irradiation the fore part of the animal was covered with gauze and a lead shield 6 mm thick; data published by Yu. G. Nefedov (1960) indicate that this ensures an entirely adequate protection of the shielded parts against biologically effective radiation.

In the acute exposure the rabbits, tied to a bench with the back facing upward, were operated on under local anesthesia. Placement of the sensor into the sincipital region took about two hours. The animal was then placed under the tube of a RUM-3 apparatus, and the initial blood flow level was recorded for a short time (15-40 min). Then the animal was irradiated, during which the recording of blood flow continued. Upon completion of exposure, the animals remained under observation for six hours, after which they were sacrificed. The rabbits were inside a box for the total irradiation.

Results

In the control group, after placement of the sensor there was a gradual decrease in the level of venous blood flow in most of the animals, attaining a maximum in the second-third hour after the operation. This phenomenon

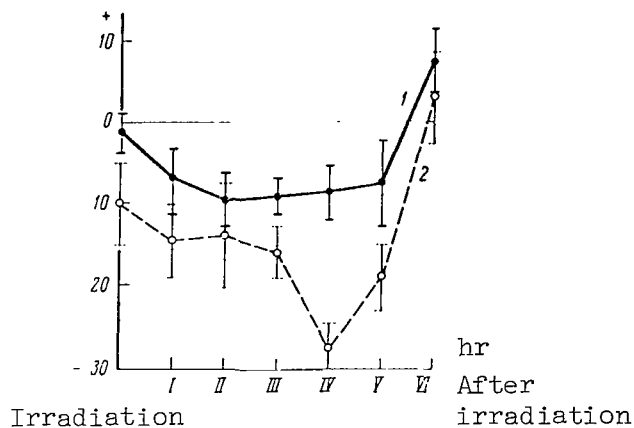


Figure 1. Blood flow in cerebral veins of rabbits in percent of initial level. 1, Control, 2, experiment. Irradiation of part of back and abdomen in acute experiment with 2000 r. Tripled errors represented by vertical lines.

apparently is related to operational trauma. We feel that there probably was an increase in intracranial pressure, developing immediately after placement of the sensor. In many animals at the end of the operation the part of the brain under the trepan opening was somewhat hyperemic and sometimes rose over the edges of the trepan opening. Under these conditions it is not impossible that there was a mechanical chiseling off of the surface veins, specifically in the region of the sensor, since its surface turned toward the brain is flat and not arched like the removed part of the bone. After three-four hours the 131 blood flow in the control animals returned to the initial level and sometimes rose above normal by the fifth-sixth hour.

The blood flow-time curve for the irradiated rabbits on the average lies lower than for the control (fig. 1), but the scatter of mean hourly data for the individual animals is great, and the difference between the experimental and control for the first two hours was statistically unreliable. In the third hour in the control the blood flow began to be reestablished, whereas in the experimental group the blood flow level on the average continued to decrease and reached a minimum value about the fourth hour after irradiation. In the third, fourth and fifth hours the blood flow in the irradiated rabbits was reliably lower than in the control group. By the sixth hour the blood flow in the experimental group and in the control increased, and the difference between the experimental and control groups became unreliable. On the whole, the entire experimental group, to judge from the median and Wilcoxon's test, differed reliably from the control at the 0.05 level.

In the chronic experiment the blood flow for two rabbits, irradiated under these same conditions (part of the back and abdomen, 2000 r), was recorded. two-four hours daily for four days prior to radiation exposure. Immediately

after irradiation, the mean level of cerebral blood flow began to decrease in both rabbits, in one animal attaining a minimum after 1 hour and in the other 2 hours after end of exposure. In seven hours of observation there was no return to the initial level. The second rabbit died on the first day after irradiation with a normal blood flow level (except for a terminal dropoff). The first rabbit survived for 10 days after irradiation and was sacrificed. On the second day the blood flow in this rabbit attained a normal level. Beginning with the sixth day there was a new decrease of the blood flow level, attaining a maximum on the seventh-eighth day (reliable difference from the control). On the ninth day the blood flow again began to be restored and by the tenth day reached normal.

Thus, in the two rabbits locally irradiated in the chronic experiment, cerebral venous blood flow decreased immediately after irradiation. This ^{/132} decrease did not reach the level of a reliable difference from the control. At later times in the surviving animal there was a second, more significant decrease of blood flow. This time, according to the blood indices, coincided with the height of radiation sickness.

Twelve preoperated rabbits were totally irradiated with 1000 r. The blood flow in these animals was first recorded for 14 days prior to irradiation. Nine animals served as control. After irradiation there was disruption of respiration (increased frequency, shortness of breath) in all animals. Seven of the 12 irradiated animals died on the day of irradiation, surviving from a half-hour to seven hours after the end of exposure. Death was caused by severe respiratory malfunctions and convulsions. Sometimes the convulsive attack and death of the irradiated animals occurred during removal of blood (two cases). Three animals died on the day following irradiation, with these same terminal phenomena. One rabbit survived for five days and died; one survived seven days and was sacrificed (the blood flow sensor malfunctioned). This high degree of mortality of the irradiated animals in our experiments and the shock character of the postradiation reaction could not be explained, and to a considerable degree made it difficult to compare our data with those given in the literature.

The mean hourly level of blood flow in the control varied from hour to hour in the range ± 5 percent of the mean level of rest; the variations had a random character. In some irradiated animals the mean level of blood flow began to decrease even during the time of irradiation. However, this did not occur in all animals. In a number of cases the blood flow immediately after irradiation was somewhat above normal. In the period which followed (from the second ^{/133} hour after end of exposure), the mean blood flow level decreased and attained a minimum in the sixth hour (fig. 2). The blood flow in the experimental group differed from the control in being statistically reliable only in the fifth and sixth hour after irradiation. By the seventh hour there was a tendency to restoration (the difference between the experiment and control became unreliable).

In three animals which died in the first hours after irradiation the blood flow increased somewhat, in two animals to the upper limit of normal. In the animals which died later the blood flow after 24 hours of irradiation remained at the lower limits of normal (disregarding the terminal decrease).

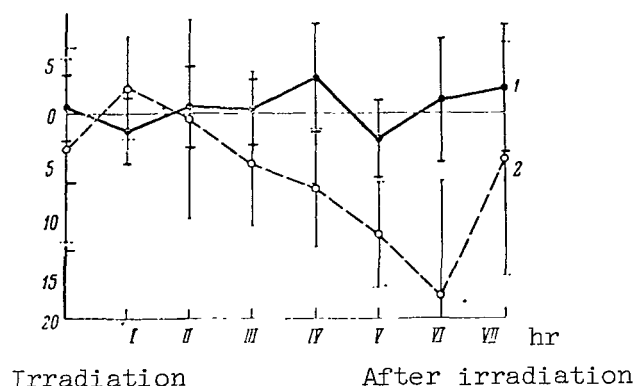


Figure 2. Blood flow in cerebral veins of rabbits in percent of initial level. 1, Control; 2, experimental. Acute whole-body irradiation in chronic experiment with 1000 r. Tripled errors represented by vertical lines.

In the two rabbits surviving for five-seven hours, the blood flow on the following days remained at a level below the control. On the second day the blood flow did not differ from normal; on the fifth day there was a second, more profound decrease. These mean diurnal deviations in the data for the two rabbits are statistically unreliable. For the entire group as a whole the difference between the experimental and control groups to judge from the median was worse than 0.05; however, the fourth-sixth hours of the first day are reliably different.

Discussion of Results

Acute irradiation of part of the back and abdomen of rabbits by 2000 r in the first hours after irradiation leads to decrease in total arterial pressure. Our data in this respect are comparable to those obtained by Yu. G. Nefedov (1955). The latter demonstrated that, with irradiation of part of the back and abdomen of rabbits with 2000 r, the maximum drop of arterial pressure occurs in the first hours after irradiation; then restoration occurs in the surviving animals. In itself a decrease in total blood pressure in animals does not lead to a proportional decrease in cerebral blood flow (Carlyle, Grayson, 1957). Recently some investigators are inclined to ascribe a great autonomy to cerebral circulation (Mchedlishvili, 1962). It was established that the system of intracranial circulation is self-regulating, that is, the blood supply level is established in accordance with the local gas balance and the functional state of a particular part of the brain tissue (Sokoloff, 1959). However, during recent years the role of extracerebral reflexes in regulation of blood circulation in the brain has been established with greater certainty than in older investigations (see Blinova and Ryzhova, 1957). It has been

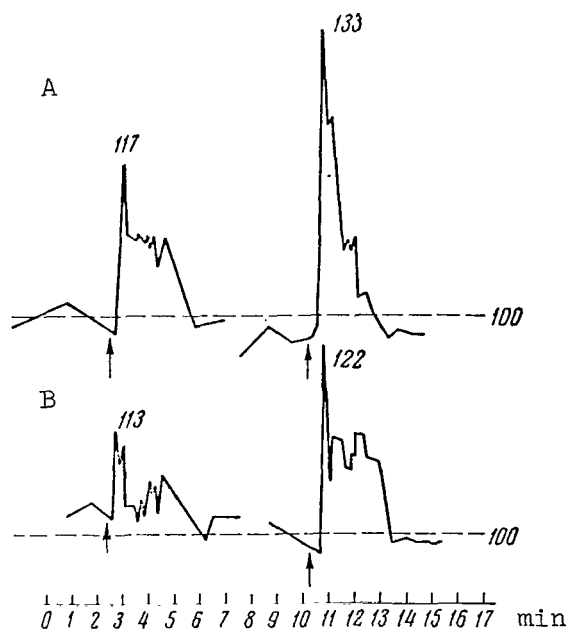


Figure 3. Reaction of cerebral venous blood flow to increase of carbon dioxide in inhaled air.

A, Prior to irradiation with 1000 r, time of administration of carbon dioxide gas in course of 10 and 20 sec; B, after irradiation, time of administration of carbon dioxide, 20 sec (twice).

demonstrated that as a result of the effect of irradiation the reactions of the brain vessels, which can cause stimulation of the extracerebral reflexogenic zones, change (Lyubimova-Gerasimova, 1962), and the general vasomotor reactions are equally modified (Lebedinskiy, 1956). In our experiments we used an admixture of 5-7 percent CO_2 to the air breathed by the animals as a

standard test of the state of the cerebral vasomotor reactions. We observed that after whole-body X-irradiation (100 r) the reaction of cerebral blood flow to the introduction of carbon dioxide becomes weaker (fig. 3).

In the light of these data the decrease in the level of cerebral venous blood flow after irradiation appears not to be the result of a decrease of total blood pressure, but the result of impairment of cerebral vasomotor reactions, caused by extracranial reflexogenic and local zones. Probably in relation to the impairment of these reflex mechanisms, the cerebral hemodynamics have a greater dependence on the level of total pressure than occurs under normal conditions. From this point of view we feel it probable that the small increase in the mean level of cerebral blood flow directly after irradiation in the group of whole-body irradiated animals is not random. In the first 10 min after irradiation some investigators note a small increase of

arterial pressure and a state of increased irritability in the irradiated animals (Nefedov, 1960). However, such an effect was not observed by Yu. G. Grigor'yev (1957).

Total irradiation had severer effects, according to the investigated index, although according to our data the maximum deterioration of blood supply to the brain during whole-body irradiation sets in later than in the case of local irradiation. In the case of local exposure in the acute experiment the tendency to restoration at the end of the period of observations is expressed more clearly. Reliable discrimination of two types of reactions, considering the existing variability, would require a considerably greater number of animals in each group. Possible differences of the mechanisms in the two considered cases could involve the presence or absence of direct radiation damage of the vasomotor center, the upper sympathetic ganglia and reflexogenic zones of the arch of the aorta and carotid sinuses. However, the dose used is scarcely sufficiently effective, according to the selected index. For detecting its influence on these systems for a given number of animals it would be convenient to use other, more specialized tests and not such an integral criterion as the rate of blood flow. In our case there is a far more obvious similarity between the observed changes in blood flow during local and whole-body irradiation. This similarity possibly is related to radiation damage in the internal organs of specific reflexogenic zones of vasomotor reactions (Lebedinskiy, 1956; Livshits, 1961; Komarov, 1957; Zaretskaya, 1956; Blinova and Ryzhova, 1957).

In experiments with whole-body irradiation of rabbits in a dose of 1000 r, R. M. Lyubimova-Gerasimova (1960) observed a slowing down of cerebral blood flow in the first hour after exposure. Normalization set in during the hours which followed. These phenomena, according to the author's observations, are related to changes in vascular tonus in the brain and the number of functioning capillaries. The first phase of the reaction in the Lyubimova-Gerasimova experiments coincides with a decrease in intracranial pressure, and the second phase coincides with an increase. The recording of the blood flow rate in these experiments was based on the time required for filling the vessels with thorotrast. In our experiments we obtained no normalization in these periods. We note the fact that for reasons not yet established the severity of the radiation damage according to external criteria and according to the mortality of the animals was considerably greater in our experiments.

Thus, according to our data, the blood flow level in cerebral veins after acute local and chronic irradiation decreased in the first hours after exposure. The maximum of decrease occurs at the fourth and sixth hour after 136 exposure for local and whole-body irradiation, respectively. It may be surmised that this decrease in the level of blood flow reflects disruption of vasomotor reactions as a result of radiation damage to links of reflex mechanisms still unknown to us. In this case the impairments of the functions of the CNS described in the literature should be regarded as secondary. However, this is not the only possible interpretation. The opposite can be assumed with equal validity: the effect of ionizing radiation directly depresses the activity of the CNS, causing a state of inhibition in the first hours after exposure to radiation (Livshits, 1961). In this case the cerebral oxygen consumption is reduced considerably in the first two-three hours after exposure (Snezhko, 1960;

Luk'yanova, 1964). From this point of view the changes in blood supply can be regarded as secondary, as the result of the depressed functional state of the CNS. This point of view appears quite justified, because the application of an oxygen load during polarographic measurement of oxygen at this time does not make it possible to detect an intensified oxygen consumption by the cerebral tissues. This means that despite the low level of blood supply no oxygen deficit is created in the cerebral tissues.

Thus, under these experimental conditions we cannot draw certain conclusions concerning the primary or secondary character of the hemodynamic changes in the CNS. The latter facts, taken together, support the idea that the observed changes in cerebral blood flow should not be regarded exclusively as a result of vasomotor disruptions. It is not impossible that these changes, at least partially, can be considered as a secondary decrease in the level of cerebral blood circulation in accordance with its current requirements.

CHARACTERISTICS OF EFFECT OF DIFFERENT TYPES OF RADIATION
ON THE HIGHER NERVOUS ACTIVITY OF SMALL ANIMALS

A. P. Korolevskiy

ABSTRACT

The comparative effect of fast neutrons, 510 MeV protons and gamma irradiation in a dose of 300 rad on the higher nervous activity of mice of the SS₅₇(Bl) strain was investi-

gated, using the motor drinking conditioned reflex method.

Exposure to these types of radiation induced disturbance of both nervous processes: excitation and inhibition. Neutron and gamma radiations led to more severe disruption of the excitation process, whereas proton radiation more seriously affected the inhibition process.

With respect to effectiveness, the three types of radiation fall on the following scale: neutron > gamma radiation > protons.

A parallelism was established between the dependence of disruption of conditioned reflex activity on linear ionization density, and the changes in the indices of the peripheral blood are described.

Comparative Effect of Fast Neutrons, Protons and Gamma
Radiation in a Dose of 300 rad (Communication I)

Much information has accumulated on the effect of different types of /138 radiation on the CNS and its functions. Various aspects of the effect of ionizing radiation on the functions of the CNS have been discussed in a number of monographs of Soviet radiobiologists (Grigor'yev, 1958, 1963; Livanov, 1962; Lebedinskiy, Nakhil'nitskaya, 1960; Livshits, 1961; Minayev, 1962; Piontkovskiy, 1964) and in the transactions of international symposia devoted to this problem (Effects of Ionizing Radiation on the Nervous System, 1962; Response of the Nervous System to Ionizing Radiation, 1962).

However, for the most part the investigations were made for the purpose of clarifying the effect of some individual types of radiation on the functions of the CNS, and we have not been able to find information on the comparative effect of radiations with different linear ionization density on these functions.

The dependence of the effect of radiations on linear ionization density has been investigated for many functions of the body (Rayevskiy, 1957). These studies are of great importance for understanding the mechanisms of the biological effect of radiation and for establishing a scientific basis for ensuring the safety of persons exposed to nuclear energy. The complete absence of data on the comparative effect of different types of radiation on higher nervous activity is an important gap in this field.

The objective of our studies conducted on the recommendation of and under the direction of N. N. Livshits, was clarification of the characteristics of the effect of different types of radiations (fast neutrons, gamma radiation and 510 MeV protons) in doses of 25, 150 and 300 rad on the higher nervous activity of mice and rats.

This communication describes the results of an investigation of the comparative effect on the conditioned reflex activity of mice exerted by fast neutrons, 510 MeV protons and gamma radiation in a dose of 300 rad. The latter is close to LD₃₀₀ for the SS₅₇ (V1) strain of mice for gamma irradiation. /139

The conditioned reflex motor method with drinking refreshment was used in the experiments. The application of the conditioned stimuli and the recording of the principal indices of the conditioned reflex reaction were accomplished with an automatic apparatus which we designed (Kornil'yev, Korolevskiy, 1963). The animal reacted to the conditioned stimulus by running to the place of refreshment (drinking bowl) along an inclined trough at an angle of 35°.

The conditioned reflex stereotype included positive conditioned stimuli -- sound and light and a differentiated sound stimulus.

The characteristics of the conditioned reflex activity for each animal were determined on the basis of 20 experiments carried out after firmly establishing the stereotype. The same number of tests was also carried out after irradiation. Exceptions were the animals irradiated by neutrons, in which subsequent to irradiation it was not possible to carry out this number of experiments, due to the appearance of indications of acute radiation sickness and the death of the animals.

The experiments were carried out on mice (sexually mature males) of the SS₅₇ (V1) strain, weighing 16-18 g. Prior to irradiation the mice were divided into four groups. Each group consisted of five animals. In distributing the animals, every care was taken to ensure that the makeup of the group, with respect to the indices of higher nervous activity, was identical. Each mouse in all groups had a partner with similar indices of higher nervous activity in each of the remaining groups. The animals without suitable partners were rejected prior to the onset of the irradiations. The groups were selected in this way in the other series of experiments as well.

The indices of conditioned reflex activity of the animals subjected to irradiation were compared with the indices of background conditioned reflex activity of these same animals, and with the corresponding indices of the animals

TABLE 1. PHYSICAL CONDITIONS OF IRRADIATION (SERIES I).

Group	Type of radiation	Dose, rad	Dose intensity, rad/hr	Animals
a	Co ⁶⁰ gamma radiation	300	1560.6	SS ₅₇ (VI) male sexually mature mice (16-18 g)
b	1.25 MeV neutrons + gamma radiation	234.8 + 64.6	258.0	Same
c	510 MeV protons	300	3348.0	Same
d	Control	-	-	Same

of the control group. Three groups of mice were subjected to general acute irradiation: one group with neutrons with a small admixture of gamma rays, another group with protons and a third with gamma rays. The fourth group of animals was not subjected to irradiation and served as control. The physical conditions of irradiation are given in table 1.

The intensity of the dose of gamma and neutron radiations was not entirely identical, but data in the literature show that this factor does not exert a sharp influence on the changes of higher nervous activity caused by irradiation (Livshits et al., 1962, 1964).

In the statistical analysis of the material, the mean values of each /140 index in any group of animals were determined from the results of 50 experiments, carried out after a day on five animals.

The changes in the principal characteristics of the positive conditioned reflex revealed attenuation of the excitation process in the animals of the irradiated groups. The only exception was the intensity of the positive conditioned reflex (running rate). In the animals irradiated by protons, this parameter increased anomalously, not correlating with lengthening of the latent period and decrease in the duration of the drinking reaction.

In mice irradiated by neutrons the latent period of the conditioned reflex lengthened sharply, but the rate of running to the place of refreshment (intensity of the conditioned reflex) decreased (figs. 1 and 2). The duration of the drinking reaction at the drinking bowl decreased insignificantly, but more than in the remaining groups (fig. 3). The number of extinctions of the conditioned reflexes increased, greatly exceeding the increase in the number of extinctions in the remaining irradiated groups, which was also evidence of strong attenuation of the excitation process (fig. 4).

In the group of animals subjected to gamma irradiation, in the first ten days after exposure there was also attenuation of the excitation process, but

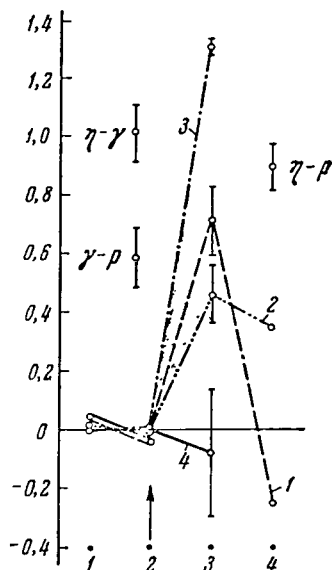


Figure 1. Mean changes of latent period of conditioned reflex after exposure to neutron, proton and gamma radiations with 300 rad. Along x-axis -- time (one point = 10 experimental days). Along y-axis -- absolute mean value of deviation from initial mean level (sec). Day of exposure denoted by arrow. Vertical lines on curves represent errors. 1, Gamma; 2, protons; 3, neutrons; 4, control.

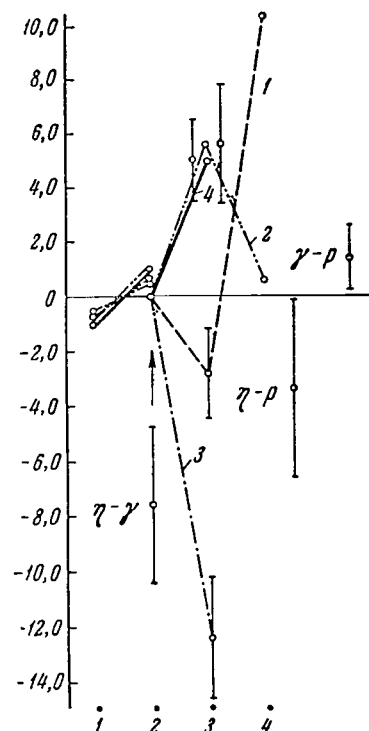


Figure 2. Mean changes of conditioned reflex after exposure to neutron, proton and gamma radiations with 300 rad. Along y-axis -- absolute mean value of deviation from initial level (cm/sec). Other notations same as in fig. 1.

it was less clearly expressed compared to the changes in the animals irradiated by neutrons. In the animals of this group the latent period of the conditioned reflex also increased in length; but the duration of the drinking reaction decreased; however, the value of the deviation was somewhat less than in animals irradiated by neutrons. The intensity of the conditioned reflex after gamma irradiation decreased to a considerably lesser degree than after exposure to neutrons. The number of extinctions of the conditioned reflex, as already mentioned, in the groups of animals subjected to gamma irradiation was considerably less than the number of extinctions in animals irradiated by neutrons. An ¹⁴¹ exception was the number of rejections of water: this exceeded the corresponding values in the groups irradiated by neutrons and protons (fig. 5).

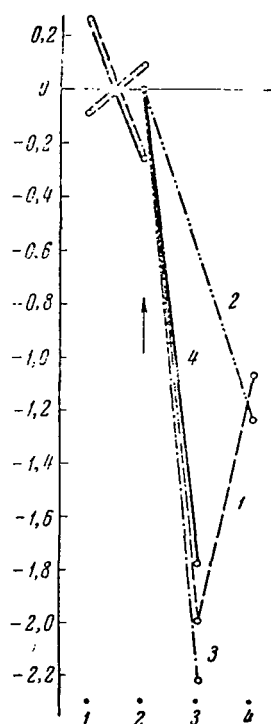


Figure 3. Mean changes of duration of drinking reaction to conditioned stimulus after exposure to neutron, proton and gamma radiations with 300 rad. Along x- and y-axes, notations same as in fig. 1. Day of exposure denoted by arrow.

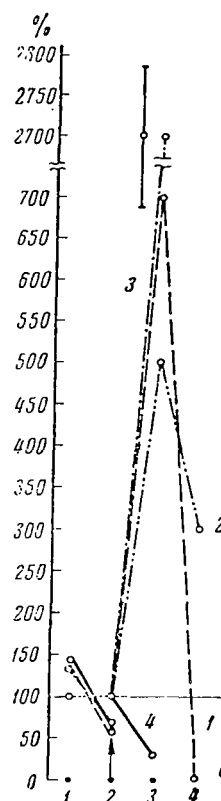


Figure 4. Changes of number of extinctions of conditioned reflex after exposure to neutron, proton and gamma radiations with 300 rad. Along y-axis -- number of extinctions of conditioned reflexes in percent of mean initial level. Other notations same as in fig. 1.

We believe that it is possible to attribute the absence of correlation between the changes in these two indices (close in value) of attenuation of the excitation process to the following factor: extinction of the conditioned motor reflex, that is, total absence of reactions to a conditioned stimulus is an indication of a severe disruption of the excitation process than only inhibition of the last link of the reflex reaction to drinking. Therefore, in mice irradiated by neutrons, in which the excitation process suffered more severely than in mice subjected to exposure to gamma rays, the first of these disruptions was observed more frequently, whereas in mice subjected to gamma irradiation the second of these disruptions was observed more frequently. /142

In the group of animals irradiated by protons, the latent period of the conditioned reflex became longer, but the duration of the drinking reaction at

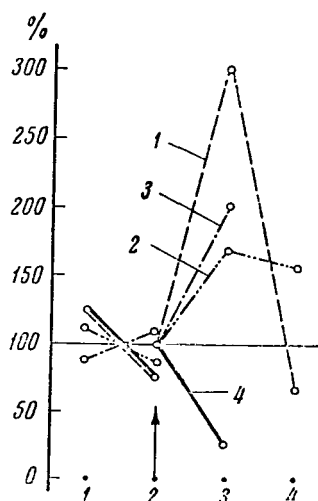


Figure 5. Changes of the number of rejections of water after exposure to neutron, proton and gamma radiations with 300 rad.

Along y-axis -- change of number of rejections of water in percent from initial mean level. Other notations same as in fig. 1.

the drinking bowl decreased. However, the deviations of the values of these indices from the mean value of the initial level were expressed to a lesser degree than observed in the animals subjected to neutron and gamma irradiations. /143

The intensity of the conditioned reflex in the group irradiated by protons, on the other hand, as already mentioned, increased somewhat. Its value almost did not differ from the intensity of the reflex in the control group of animals (fig. 2). The increase in the number of extinctions of the conditioned reflex in this group, as well as rejections of water, was less significant than in mice subjected to gamma irradiation. These relations differ somewhat from those established in our earlier comparison of the results of neutron and gamma irradiations.

In the animals irradiated by neutrons, as mentioned above, more severe disruptions of higher nervous activity -- extinction of the conditioned reflex -- was observed more frequently, whereas among the mice subjected to gamma irradiation it was more common to observe a less severe disruption of higher nervous activity -- rejection of water. In the group irradiated by protons, both types of impairments of higher nervous activity appeared less frequently than in the group subjected to exposure to gamma rays. Attenuation of the excitation process in the first of these groups was least clearly expressed. /144

In the control group the deviations of the values of the different indices from the mean initial level either were very insignificant or indicated an improvement of the excitation process. The latent period decreased, virtually remaining at the lower limit of the initial level, but the rate of running to the place of refreshment increased to the level of deviation of this index in the group of animals subjected to exposure to protons. Only the duration of the drinking reaction decreased to the same value as in the group of animals subjected to gamma irradiation. The number of extinctions of the conditioned reflex and the number of rejections of water in the control mice, compared to the mean level before irradiation, decreased and contrasted with the sharp increase of these indices in the irradiated groups of animals. We assume that such a decrease in the values of these two indices is the result of conditioning. /145

In all irradiated animals there was an increase in the number of phase phenomena. This was expressed most sharply in the animals subjected to exposure to neutrons. In this group there was an increase of the number of adjustment and paradoxical phases, with respect to the index of mean duration of the latent period of conditioned reflexes. After gamma irradiation the increase of the number of phase phenomena was less clearly expressed than in animals irradiated by neutrons. There was a still less significant disruption of the proper force relationships in the group of mice irradiated by protons.

In the control group the number of paradoxical phases decreased insignificantly, but the number of adjustment phases remained unchanged (figs. 6 and 7).

The reactions to differentiation in the animals irradiated by neutrons decreased with respect to all indices. The latent period of the reaction to a differentiated stimulus increased, but the running rate and the duration of the drinking reaction decreased (figs. 8, 9 and 10).

In the group of animals subjected to gamma irradiation, the latent period of differentiated reaction decreased, which indicated some disinhibition of differentiation, but the running rate and the duration of the drinking reaction to the differentiated stimulus also decreased, which seemingly was evidence of improvement of differentiation.

In the group of animals irradiated by protons, the latent period of differentiated reaction revealed a stronger disinhibition, but the intensity of the differentiated reaction revealed an improvement of differentiation, more clearly expressed than in the group of animals subjected to gamma irradiation. As in the other groups of animals, the duration of the drinking reaction to a differentiated stimulus in mice irradiated by protons also decreased, revealing some deepening of differentiation, but expressed to a lesser degree than in the other groups. These observations show that in the group of animals subjected to proton and gamma irradiations there is a correlation in the direction of the changes of the latent period and the intensity of the reaction to a differentiated signal. Whereas in both groups the decrease of the latent period indicated a disinhibition of differentiation, the intensity of the reflex to a differentiated signal revealed a deepening of it.

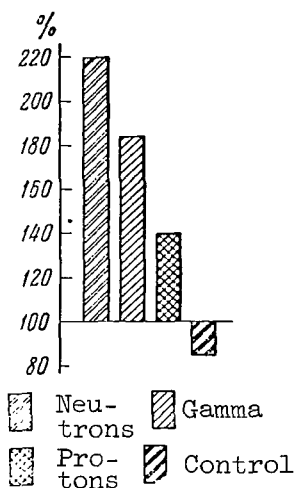


Figure 6. Changes of relative number of paradoxical phases after exposure to neutron, proton and gamma radiations with 300 rad.

Along y-axis -- number of paradoxical phases in percent of mean initial level.

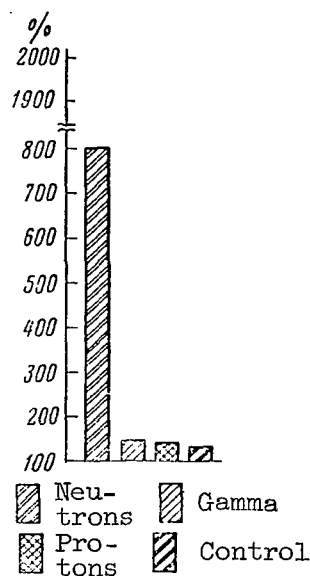


Figure 7. Changes of relative number of adjustment phases after exposure to neutron, proton and gamma radiations with 300 rad.

Along y-axis -- number of adjustment phases in percent of mean initial level.

It is clearly noted that in the control group the duration of the drinking reaction after a differentiated stimulus decreased almost to the same degree as in the groups subjected to neutron and gamma irradiation which in all probability, is the result of conditioning. Therefore, we received the impression that irradiation with 300 rad is almost no obstacle to the process of conditioning in these animals. These results differ from the effects of irradiation with 25 rad. As will be demonstrated in one of our next communications, exposure to 25 rad complicated the formation of differentiation with respect to this index, which was especially clearly expressed in mice irradiated by neutrons. In animals irradiated by neutrons the protective inhibition was expressed most sharply, and the phenomenon of disinhibition of differentiation was therefore not detected. We will attribute this phenomenon to the fact that under the influence of irradiation there is attenuation of both excitation and inhibition processes. With respect to a number of indices the attenuation of the inhibition process is masked by the development of protective inhibition and its summation with conditioned inhibition. Such an explanation on the basis of similar phenomena was proposed for the first time by A. V. Lebedinskiy and Z. N. Nakhil'nitskaya (1960). It remains unclear why the disruption of differentiations in mice exposed to proton and gamma irradiations was not

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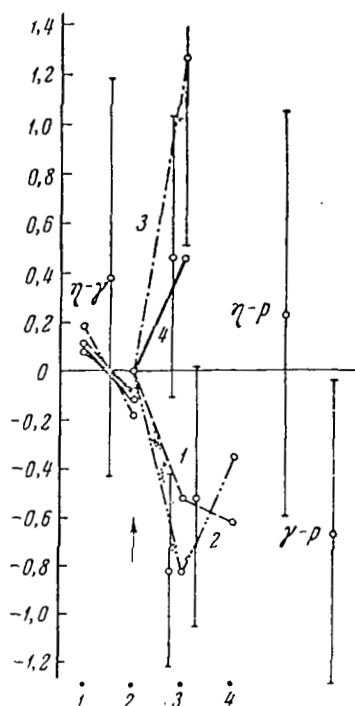


Figure 8. Mean changes in latent period of relative differentiation after exposure to neutron, proton and gamma radiations with 300 rad. Notations same as in fig. 1.

discovered on the basis of the difficult criterion, duration of the alimentary reaction, but on the basis of the easier criterion, the value of the latent period. At present we cannot explain the reasons for this phenomenon, but we assume that the changes of differentiation which we observed are related to the effect of two factors: attenuation of conditioned inhibition and development of protective inhibition, which can be combined in different ways. Table 2 presents the results of statistical analysis of the data obtained in this series of experiments, using the Student test.

Table 2 shows that despite the small number of animals, differences between changes in the two principal indices of the conditioned reflex after exposure to different types of radiation were reliable.

We carried out four series of experiments in which a study was made of the effect of these types of radiations on higher nervous activity.

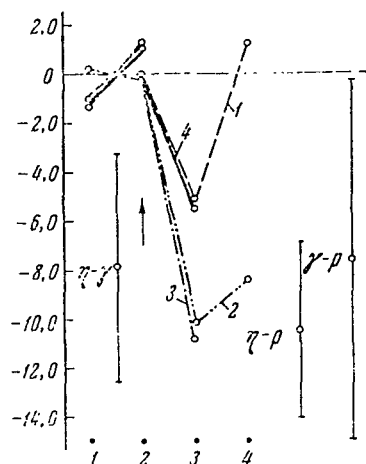


Figure 9. Mean changes in running rate in response to differentiated stimulus after exposure to neutron, proton and gamma radiations with 300 rad. Along y-axis -- absolute mean value of deviations from initial mean level (cm/sec). Other notations same as in fig. 1.

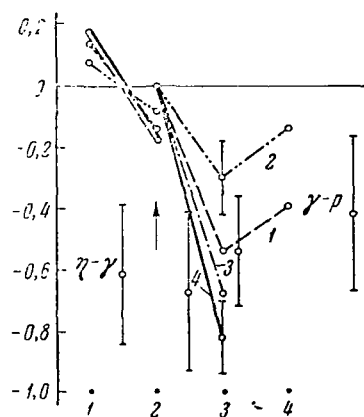


Figure 10. Mean changes in duration of drinking reaction in response to differentiated stimulus after exposure to neutron, proton and gamma radiations with 300 rad. Notations same as in fig. 1.

TABLE 2. PROBABILITY OF RANDOM DISCREPANCIES OF MEAN VALUES (STUDENT TEST).

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Index of conditioned reflex activity	Compared types of radiations	Probability of random discrepancy (P)
Latent period of conditioned reflex	n-γ	P < 0.05
	p-γ	P > 0.05
	n-p	P < 0.05
Intensity of conditioned reflex	n-γ	P > 0.05
	p-γ	P > 0.05
	n-p	P < 0.01
Duration of drinking reaction after conditioned stimulus	n-γ	P > 0.05
	p-γ	P > 0.05
	n-p	P > 0.05
Latent period of relative differentiated reaction	n-γ	P > 0.05
	p-γ	P > 0.05
	n-p	P > 0.05
Intensity of relative differentiated reaction	n-γ	P > 0.05
	p-γ	P > 0.05
	n-p	P > 0.05
Duration of drinking reaction to differentiated stimulus	n-γ	P > 0.05
	p-γ	P > 0.05
	n-p	P > 0.05
No. of cases of absent conditioned reflex	n-γ	P < 0.05
	p-γ	P > 0.05
	n-p	P < 0.001
No. of cases of rejection of drink	n-γ	P > 0.05
	p-γ	P > 0.05
	n-p	P > 0.05
No. of paradoxical phases (for duration of latent period of conditioned reflex)	n-γ	P > 0.05
	p-γ	P > 0.05
	n-p	P > 0.05
No. of adjustment phases (for this same index)	n-γ	P < 0.001
	p-γ	P > 0.05
	n-p	P < 0.01

TABLE 3. PHYSICAL CHARACTERISTICS OF IRRADIATION AND EXPERIMENTAL ANIMALS.

Group	Type of irradiation	Dose, rad	Dose intensity, rad/hr	Animals
a	Co ⁶⁰ gamma radiation	300.0	1560.6	SS ₅₇ (V1) mice, males, 16-18 g
b	1.25 MeV neutrons + gamma radiation	234.8 + 64.6	258.0	Same
c	510 MeV protons	300.0	3348.0	Same
a	Co ⁶⁰ gamma radiation	25	360.0	Same
b	1.25 MeV neutrons + gamma radiation	19.5 + 5.5	258.0	Same
a	Co ⁶⁰ gamma radiation	150.0	1320.0	BAL V male mice, 16-18 g
b	1.25 MeV neutrons + gamma radiation	131.0 + 19.0	795.0	Same
a	Co ⁶⁰ gamma radiation	150.0	1230.0	"August" rats, males, 150-180 g
b	1.25 MeV neutrons + gamma radiation	107.0 + 42.0	236.0	Same
c	510 MeV protons	150.0	3348.0	Same

Information on the physical conditions of exposure and the experimental 147 animals is given in table 3. The results of each of the series of experiments will be published separately.

It is only necessary here to note that summary data for the four series were analyzed with Wilcoxon's test. As is well known, this test is non-parametric and can be used for analyzing nonuniform data, provided the makeup of the compared groups is identical. The measures taken to ensure satisfaction of this condition were mentioned previously. The results of the statistical processing are given in table 4.

Table 4 shows that in the analysis of summary data the differences in the latent period of running in response to a differentiated stimulus were reliable.

During the period of the investigation four blood analyses were made for each animal. In all samples of the group irradiated by neutrons leukopenia was expressed more sharply than in the remaining experimental groups (fig. 11). On the second day after irradiation the number of leukocytes in this group of animals decreased by almost 7,500 cells below the mean initial level; on the

TABLE 4. PROBABILITY OF RANDOM DISCREPANCIES OF MEAN VALUES (WILCOXON'S TEST).

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Index of conditioned reflex activity	Compared types of radiations	Probability of random discrepancy (P)
Latent period of conditioned reflex	n- γ	P < 0.05
	p- γ	P < 0.05
Intensity of conditioned reflex	n- γ	P > 0.05
	p- γ	P < 0.01
Duration of drinking reaction after conditioned stimulus	n- γ	P > 0.05
	p- γ	P > 0.05
Latent period of relative differentiated reaction	n- γ	P < 0.05
	p- γ	P < 0.05
Intensity of relative differentiated reaction	n- γ	P > 0.05
	p- γ	P > 0.05
Duration of drinking reaction to differentiated stimulus	n- γ	P < 0.05
	p- γ	P > 0.05

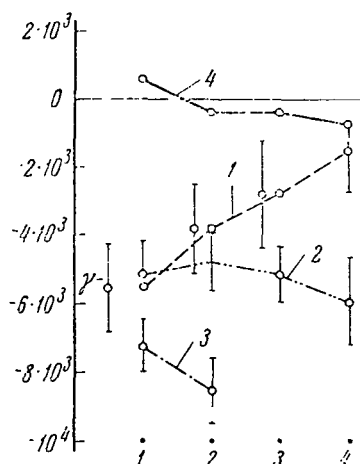


Figure 11. Dynamics of changes in content of leukocytes in peripheral blood after exposure to neutron, proton and gamma radiations with 300 rad. Along x-axis -- time in weeks. Along y-axis -- absolute mean deviation of number of cells from initial mean level. Vertical lines on curves represent errors of mean values. Other notations same as in fig. 1.

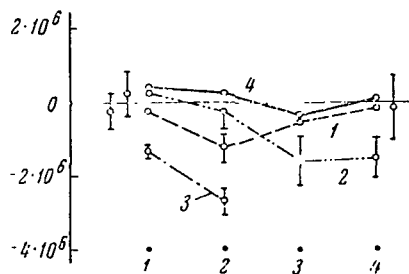


Figure 12. Dynamics of changes in content of erythrocytes in peripheral blood after exposure to neutron, proton and gamma radiations with 300 rad. Notations same as in fig. 11.

eighth day there was a decrease by almost 9,000 cells. Subsequent to this time, further blood analyses for this group of animals had to be dispensed with, due to onset of death.

In the groups of animals subjected to proton and gamma irradiations the number of leukocytes on the second day after exposure decreased by 5,000 ^{/148} and 5,500 cells respectively from the mean normal. The restoration of the normal number of leukocytes in the group of animals subjected to gamma irradiation proceeded intensively, and by the 22nd day after exposure the number of leukocytes was 1,600 cells less than the mean norm. However, in the group of animals irradiated by protons there was no restorative process at all.

However, here, after an almost insignificant initial tendency to restoration, after the second analysis there was a constant smooth decrease of the number of leukocytes. In the control group the number of leukocytes varied from +0.5 to -0.8 thousand cells of the mean initial level, which does not exceed the ordinary fluctuations of this index among mice.

The change in the number of erythrocytes was not as substantial (fig. 12). The number of erythrocytes in the group irradiated by neutrons decreased by the second day after exposure by 1,500,000 cells from the mean ^{/150} initial value, and by the eighth day, by 2,700,000 cells. In the group of mice subjected to proton and gamma irradiations the decrease of the content of erythrocytes did not differ appreciably from their fluctuations at the norm.

The results of analyses of the peripheral blood were also subjected to statistical analysis with Student's test for this series (table 5) and using Wilcoxon's test for the summary data of four series (table 6).

Table 5 shows that the differences in the changes of the content of leukocytes in animals subjected to gamma and neutron and neutron and proton irradiations were reliable in the individual tests. With respect to this index,

TABLE 5. PROBABILITY OF RANDOM DISCREPANCIES OF MEAN VALUES OF CONTENT OF LEUKOCYTES AND ERYTHROCYTES IN PERIPHERAL BLOOD USING STUDENT'S TEST (300 rad).

Com- pared type of ra- diation	Leukocytes (samples)				Erythrocytes (samples)			
	I	II	III	IV	I	II	III	IV
n-γ	P>0.05	P>0.05			P>0.05	P>0.05		
p-γ	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05
n-p	P>0.05	P<0.05			P>0.05	P<0.05		

NOTE. Selection of pairs of animals was made prior to irradiation. Absolute observational data were analyzed.

TABLE 6. PROBABILITY OF RANDOM DISCREPANCIES OF MEAN VALUES OF CONTENT OF LEUKOCYTES AND ERYTHROCYTES IN PERIPHERAL BLOOD (ANALYSES OF SUMMARY DATA FOR FOUR SERIES USING WILCOXON'S TEST).

Com- pared type of ra- diation	Leukocytes (samples)				Erythrocytes (samples)			
	I	II	III	IV	I	II	III	IV
n-γ	P<0.01	P<0.01	P<0.01	P<0.01	P<0.01	P<0.01	P<0.01	P<0.01
p-γ	P<0.05	P<0.01	P>0.05	P<0.01	P<0.01	P>0.05	P>0.05	P>0.05
n-p	P<0.01	P<0.01	P<0.01	P>0.05	P<0.01	P<0.01	P<0.01	P<0.01

the differences among the groups subjected to proton and gamma irradiations were not reliable for any time during the investigation. The differences in the content of erythrocytes among both irradiated groups were reliable only in the second observation period.

Analysis of the summary data for the four series revealed that the differences between the cell content of both white and red blood cells in all irradiated groups were reliable in the overwhelming majority of the tests.

Thus, there is a considerable correspondence between the severity of /151 the disruptions of higher nervous activity and the vulnerability of the blood system during exposures to the above-mentioned types of radiations.

Conclusions

1. Acute whole-body exposure of mice of the SS₅₇ (VI) strain to a radiation dose of 300 rad by fast neutrons, gamma rays (Co⁶⁰) and 510 MeV protons caused changes in conditioned motor drinking reflexes which were dissimilar in value, and according to some indices -- also dissimilar in direction. With respect to the effectiveness of exposure, these types of radiations fall in the series: neutrons > gamma radiation > protons.

2. Neutron and gamma irradiations caused attenuation of excitation processes, manifested in an increased latent period of positive reflexes, decreased intensity of the conditioned reflex, an increase in the number of cases of absent conditioned reflexes, and disruption of the proper force relationships. All these phenomena were more substantial in animals irradiated by protons than in animals exposed to gamma irradiation. /152

Relative to the principal indices, proton irradiation caused changes in the same direction, but less severe than gamma irradiation. An exception was the intensity of the conditioned reflex which increased, not corresponding to the decreased duration of the drinking reaction and the increased latent period of the conditioned reflex.

3. Neutron irradiation led to intensified differentiations with respect to all indices of these reactions, which in our opinion was caused by a summation of protective and conditioned inhibitions. After gamma and proton irradiations, in addition to intensified differentiation for some of the indices (running rate, duration of drinking reaction), there was disinhibition of differentiation according to the latent period index. Disinhibition was more clearly expressed in animals irradiated by protons.

4. Exposure to the investigated types of radiations caused disruptions of both nervous processes. Neutron and gamma irradiation more strongly damaged the excitation process while proton irradiation caused greater disruption of the inhibition process. It is possible that the disruption of the inhibition process in animals irradiated by neutrons was masked by the development of protective inhibition.

5. The leukopenic reaction was expressed most sharply in animals irradiated by neutrons. The process of restoration of the number of leukocytes in the peripheral blood after gamma irradiation was rather active. In the group of animals irradiated by protons, the number of leukocytes after exposure to radiation did not give any indication of restoration. Thus, in this series of experiments the expected parallelism between the dependence on linear ionization density and the damaging effect of radiations on higher nervous activity and blood is confirmed with respect to most indices.

CHARACTERISTICS OF EFFECT OF DIFFERENT TYPES OF RADIATION ON THE HIGHER NERVOUS ACTIVITY OF SMALL ANIMALS

A. P. Korolevskiy

ABSTRACT

A study was made of the comparative effect of fast neutrons and gamma irradiation (Co^{60}) in a dose of 25 rad on the higher nervous activity of mice, employing the conditioned reflex drinking method.

It is demonstrated that acute whole-body neutron and gamma irradiations induced weakening of the processes of inhibition and stimulation. Weakening of the processes of active inhibition and stimulation in mice exposed to neutron irradiation was expressed more clearly than in animals exposed to gamma irradiation.

It was found that there is a parallelism between disruptions of conditioned reflex activity depending on linear ionization density, and changes in the hematological indices were observed.

Comparative Effect of Fast Neutrons and Gamma Radiation in a Dose of 25 rad (Communication II)

In the preceding communication we presented the results of an investigation of the comparative effect of fast neutrons, 510 MeV protons and gamma radiation in a dose of 300 rad on the conditioned reflex activity of mice. These types of radiation in an identical dose caused changes in the conditioned alimentary reflexes which were dissimilar in value, and according to some indices, also dissimilar in direction. The effects of neutron and gamma radiation led to relatively greater damage to the stimulation process and the proton irradiation to relatively greater damage to the inhibition process. The changes of conditioned reflex activity in mice subjected to neutron irradiation were severer than in the group of animals subjected to the effect of gamma radiation in an equal dose. The presence of the same relations between the changes of the composition of the peripheral blood of the compared groups of animals was also demonstrated. In general, the decrease of the number of leukocytes and erythrocytes was more significant if ionization density was more linear. /154

Thus, a parallelism was established between the severity of the reaction of the nervous system to irradiation and the degree of change of the morphological composition of the peripheral blood depending on the linear ionization density. It was also discovered that the dependence of different indices of conditioned reflex activity on the linear ionization density is not the same.

The objective of this study was a comparative investigation of the influence exerted on the conditioned reflex activity of mice by exposure to fast neutrons and gamma radiation in a dose of 25 rad. The research method was de-

scribed in detail in the preceding study¹. Here we repeat only briefly that we investigated the effect of radiation on the conditioned drinking reflexes /155 (running upward to a drinking bowl along an inclined plane). The latent period of the reaction, running rate and duration of the drinking reaction were recorded automatically by a previously described method (Kornil'yev, Korolevskiy, 1963). The work was done with a stereotype, including sound (strong) and light (weak) conditioned stimuli and one differentiation in the auditor analyzer. The animals were subjected to irradiation after firm establishment of positive conditioned reflexes and formation of relative differentiation. The experimental groups of mice (five animals in each group) were subjected to a whole-body acute irradiation by neutrons and gamma radiation. The third group of animals served as control. As in the preceding study, in the distribution of animals by groups special care was taken that the makeup of the groups was identical. Each animal in one group had one partner with similar indices of conditioned reflex activity in each of the remaining groups.

The physical conditions of irradiation are given in table 1.

In the groups of animals subjected to irradiation, the direction of the changes of conditioned reflex activity, according to most of the indices, was identical, and only the degree of disruption was dependent on the linear ionization density.

The changes of the latent period of the conditioned reflex, running rates and number of extinctions of the conditioned reflex in both irradiated groups were evidence of attenuation of the stimulation process. The latent period increased considerably, but the running rate decreased somewhat in comparison with the mean initial level (figs. 1 and 2). In the control group the latent /156 period of the conditioned reflex at this same time decreased a little, but the running rate did not change. In the animals irradiated by neutrons the changes of both indices were expressed less clearly than in animals subjected to gamma irradiation. It also should be noted that in mice subjected to exposure to gamma rays the latent period in the second 10-day period was shorter, and the running rate was greater than prior to irradiation. This phase of improvement of several indices of higher nervous activity after irradiation has repeatedly been described in the literature (Nemenov, 1944, 1950; Lebedinskiy,

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See our preceding article in this collection.

TABLE 1. PHYSICAL CONDITIONS OF IRRADIATION AND EXPERIMENTAL ANIMALS (Series II).

Group	Type of radiation	Dose, rad	Dose intensity, rad/hr	Animals
a	Co ⁶⁰ gamma radiation	25	360.0	SS ₅₇ (V1) male sexually mature mice (16-18 g)
b	1.25 MeV neutrons + gamma radiation	19.5 + 5.5	258.0	Same
c	Control	-	-	Same

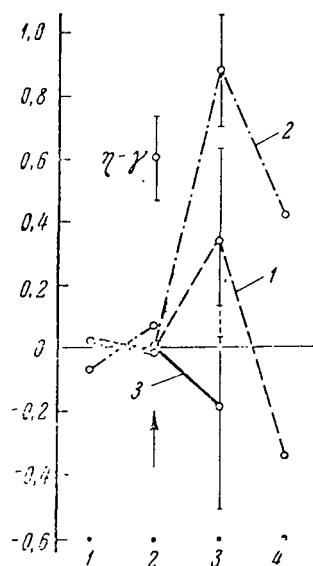


Figure 1. Mean changes of latent period of conditioned reflex after exposure to neutron and gamma radiations (25 rad). Along x-axis -- time (one graduation = 10 experimental days). Along y-axis -- absolute mean value of deviation from initial mean level (sec). Day of exposure indicated by arrow. Vertical lines on curves represent errors of mean values. 1, gamma; 2, neutron; 3, control.

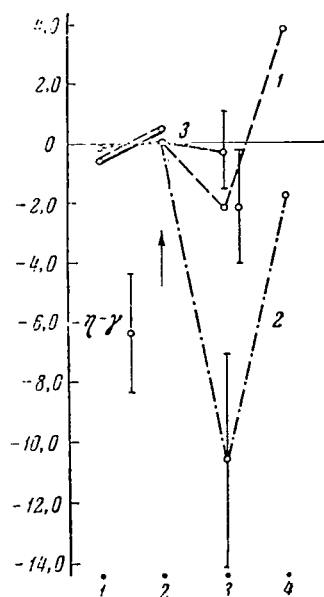


Figure 2. Mean changes of intensity of conditioned reflex after exposure to neutron and gamma radiations (25 rad). Along y-axis -- absolute mean value deviation from initial mean level (cm/sec). Other notations same as in fig. 1.

Nakhil'nitskaya, 1960; Livshits, 1956, 1961; Lomonos, 1957; Meyzerov, 1959, 1962; Blair, 1958; Riopelle, 1956, and others), and we cannot discuss its /157 mechanism here.

It should be noted that in animals irradiated by neutrons the phase of improvement of these indices was not observed. The latent period of the conditioned reflex, although somewhat decreased in comparison with that recorded in the first 10-day period, did not reach the initial level, and the running rate did not exceed normal limits (figs. 1 and 2).

Differences between the changes of the latent period and the intensity of the conditioned reflex in animals subjected to neutron and gamma irradiation were clearly expressed, but not reliable.

Duration of the drinking reaction after exposure to a conditioned stimulus was a less sensitive index and was virtually identical in the irradiated and control groups (fig. 3).

The number of extinctions of the conditioned reflex (cases of lacking reaction to a conditioned stimulus) also increased in both irradiated groups and decreased considerably in the control group. The maximum increase of the /158 number of cases lacking a conditioned reflex was discovered in mice

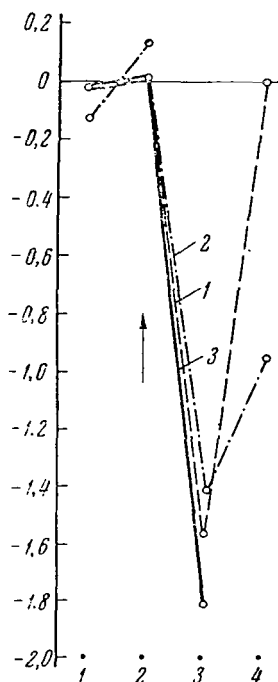


Figure 3. Mean changes of duration of drinking reaction to conditioned stimulus after exposure to neutron and gamma radiations (25 rad). Along x- and y-axes, notations same as in fig. 1. Day of exposure is denoted by arrow.

irradiated by neutrons (fig. 4). In mice subjected to gamma radiation, in the second 10-day period the number of cases lacking a conditioned reflex decreased and was below the initial level. In mice irradiated by neutrons there was no improvement of the higher nervous activity according to this index.

In animals subjected to irradiation there also was an increase of the number of cases of rejection of drinking reinforcement. It should be noted that, in contrast to the number of extinctions of the conditioned reflex, an increase of the number of cases of rejection of drinking when the animal reached the drinking bowl and returned without drinking was expressed more sharply in mice subjected to exposure to gamma rays than in mice irradiated with neutrons. The difference was not reliable, $P > 0.05$ (fig. 5).

A possible explanation of the absence of correlation of changes of the number of extinctions of conditioned reflexes and the number of rejections of drinking reinforcement was presented in the preceding study, because similar phenomena were observed under the influence of neutrons and gamma radiation

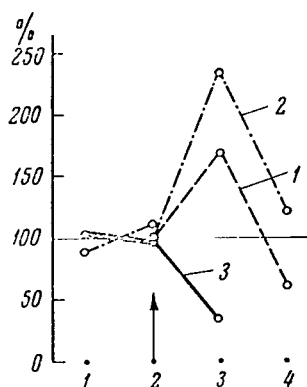


Figure 4. Changes of number of extinctions of conditioned reflex after exposure to neutron and gamma radiations (25 rad).

Along y-axis -- number of extinctions of conditioned reflexes, expressed in percent of initial level. Other notations same as in fig. 1.

and in the case of irradiation in a dose of 300 rad. We postulated that the total absence of a reaction to a conditioned stimulus is a severer disruption of the stimulating process than inhibition of only the last link of this reaction -- the natural drinking reflex. Therefore, in the animals irradiated by neutrons, in which the stimulation process was attenuated to a greater extent than in animals subjected to gamma irradiation, the first of these disruptions was observed more frequently; after gamma irradiation the second was observed more frequently. After neutron irradiation a small improvement was observed in the second 10-day period only with respect to this index.

The changes of the latent period of the reaction and the running rate in response to the differentiated stimulus indicated some tendency to intensification of differentiation after neutron irradiation and the phenomenon of disinhibition after gamma irradiation. In the first of these groups the latent /159 period of the reaction to differentiation lengthened somewhat, and the running rate decreased. Gamma irradiation had the opposite effect. In the control group these indices remained virtually unchanged. Therefore, by the time of irradiation they already were quite stable. Different relations were discovered in the changes of duration of the drinking reaction after running in response to the differentiated stimulus. When the animal reached the drinking bowl, a whole series of positive conditioned stimuli (appearance of part of the groove where the drinking bowl was situated appearance of the drinking bowl, etc.) acted on the animal. Therefore, the extinction of the reaction to these stimuli was a difficult problem. Prior to irradiation the inhibition of this reaction still was not stabilized, and conditioning continued after irradiation. This was confirmed by the fact that in the control group, in the course of the first 10-day period after irradiation of the experimental groups, the duration of the drinking reaction decreased by more than a factor of 3.

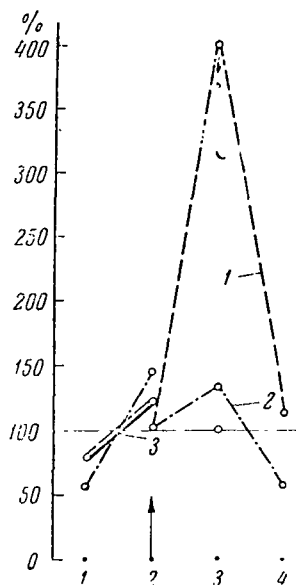


Figure 5. Changes of number of rejections of water after exposure to neutron and gamma radiations (25 rad). Along y-axis -- number of rejections of water, expressed in percent of initial mean level. Other notations same as in fig. 1.

Both irradiated groups were less capable of conditioning, and this was expressed more strongly in the animals irradiated by neutrons. This indicates a defective character of active inhibition, according to this index, in the irradiated animals, especially sharply expressed in the group subjected to exposure to neutrons. Lengthening of the latent period and decrease of the running rate in response to a differentiated stimulus apparently was caused in these mice by by summation of protective and conditioned inhibitions. The possibility of this process in animals subjected to irradiation was pointed out by A. V. Lebedinskiy and Z. N. Nakhil'nitskaya (1960).

As previously mentioned, the differences in the changes of the latent period and the intensity of the conditioned reflex after neutron and gamma irradiations were not reliable on the basis of Student's test.

In the preceding communication we mentioned that we made four series of experiments for comparing the effect of neutron, proton and gamma irradiations on conditioned reflex activity. This report presents the results of only one of these series, in which the effects of neutron and gamma irradiations are compared.

A number of indices indicate that the radiation effects had an identical direction in all four series. Summary data for these indices were processed

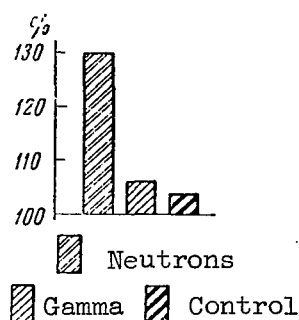


Figure 6. Changes of number of paradoxical phases after exposure to neutron and gamma radiations (25 rad). Along y-axis -- number of paradoxical phases, expressed in percent of mean initial level.

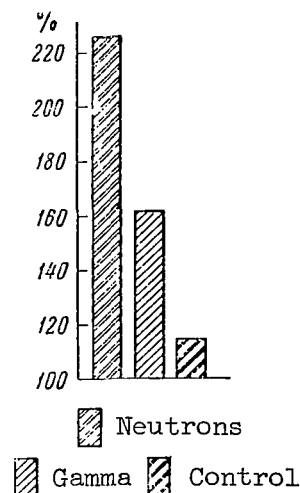


Figure 7. Changes of number of adjustment phases after exposure to neutron and gamma radiations (25 rad). Along y-axis -- number of adjustment phases, expressed in percent of mean initial level.

with Wilcoxon's test. The differences in the changes of the latent period of the differentiated reaction and the duration of the drinking reaction in response to the differentiated stimulus after neutron and gamma irradiations were reliable with respect to the summary data.

In the irradiated mice the phenomena of protective inhibition actually were present. This was confirmed by an increase of the number of phase phenomena.

The increase of the number of phase phenomena (according to the index 160 of the duration of the latent period of conditioned reflexes) was expressed most sharply in mice irradiated by neutrons (figs. 6 and 7). The difference was not statistically reliable, but qualitatively the differences were the same as in the two remaining series of experiments (see article in this collection), which makes it possible to consider these results as nonrandom. This indicates that the phenomena of protective inhibition were most sharply expressed in mice irradiated by neutrons. Therefore, the intensification of differentiations (figs. 8 and 9) in this group can be attributed to the summation of the protective and conditioned inhibitions, whereas the process of active inhibition in these animals, as mentioned before, remained defective. In mice subjected to gamma radiation the protective inhibition was expressed more weakly. This is indicated by the lesser change of the latent periods of positive conditioned reflexes and a lesser number of phase phenomena. Therefore, the attenuation of active inhibition in the animals of this group was manifested more clearly,

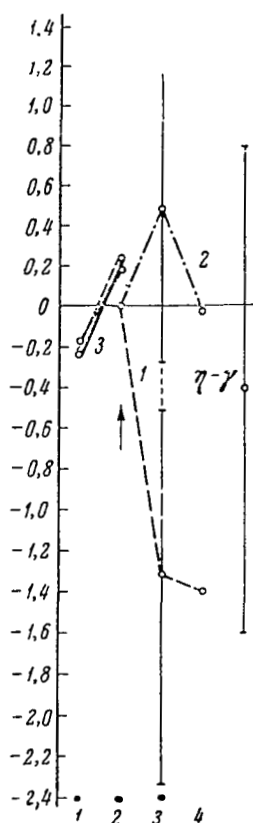


Figure 8. Mean changes of latent period of relative differentiation after exposure to neutron and gamma radiations (25 rad). Notations same as in fig. 1.

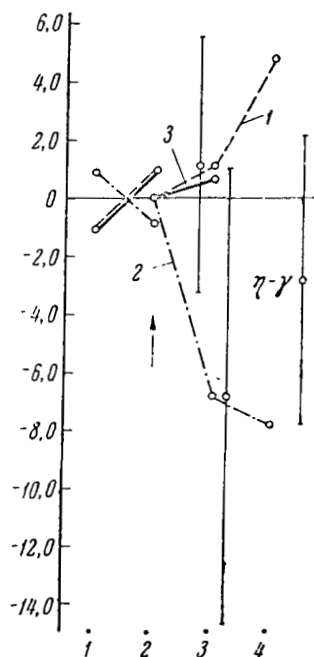


Figure 9. Mean changes of running rate in response to differentiated stimulus after exposure to neutron and gamma radiations (25 rad). Along y-axis -- absolute mean value of deviation from initial mean level (cm/sec). Other notations same as in fig. 1.

because it was masked by the protective inhibition to a lesser degree. The fact that the number of intersignal outputs in the irradiated groups decreased more significantly apparently can be attributed to the summation of protective and conditioned inhibitions. In the mice irradiated by neutrons the decrease of the number of intersignal outputs was maximum.

In other words, the effect of neutron and gamma irradiations caused /161 attenuation of both nervous processes: inhibition and stimulation. However, the protective inhibition and its summation with conditioned inhibition masked the attenuation of the latter. This process of masking attenuation of conditioned inhibition by protective inhibition was more sharply expressed in animals irradiated by neutrons. Attenuation of conditioned inhibition could be

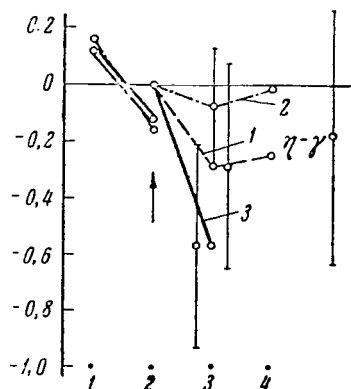


Figure 10. Mean changes of duration of drinking reaction in response to differentiated stimulus after exposure to neutron and gamma radiations (25 rad). Notations same as in fig. 1.

detected only on the basis of the index of duration of the drinking reaction in response to the differentiated stimulus -- the most difficult criterion, requiring stresses of the inhibition process (fig. 10).

Thus, in mice subjected to the effect of neutrons, the disruption of /162 higher nervous activity, according to most of the indices, was more severe than in mice irradiated by gamma rays in the same dose.

The same relations were also discovered in the changes of hematological indices. The decrease of the number of leukocytes and erythrocytes in mice irradiated by neutrons was more significant than in the group subjected to the effect of gamma radiation. By the time of the first test (on the next day after irradiation) the number of leukocytes had decreased by 5,000 cells from the mean initial level (fig. 11). In the second and third tests there was some progressive intensification of leukopenia, and only after the third test was there beginning of restoration (although incomplete) of the number of leukocytes.

In the group of animals subjected to gamma irradiation, the number of leukocytes in the first test had decreased by only 3,000 from the mean initial number. In the second test (on the 8th day) it decreased by another 1,000 cells. The process of restoration was incomplete; by the end of the observation period the number of leukocytes in this group of animals remained less than the initial value by 2,500 cells.

In the case of irradiation with 25 rad, as in the case of exposure to /163 300 rad, the control was the same group of animals. As mentioned in the first communication, the changes of the number of leukocytes in the control group did not exceed the limits of ordinary fluctuations of this index in healthy animals.

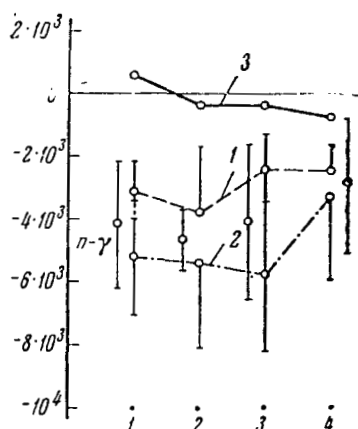


Figure 11. Dynamics of changes of content of leukocytes in peripheral blood after exposure to neutron and gamma radiations (25 rad).

Along x-axis -- time in weeks. Along y-axis -- absolute mean deviation of number of cells from initial mean level (number of cells per 1 mm^3). Vertical lines on curves represent errors of mean values.

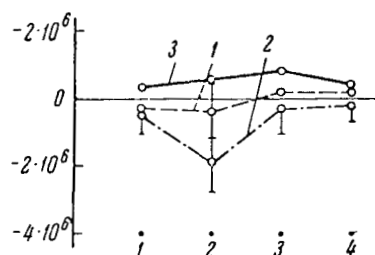


Figure 12. Dynamics of changes of content of erythrocytes in the peripheral blood after exposure to neutron and gamma radiations (25)rad. Notations same as in fig. 11.

A decrease of the number of erythrocytes was observed only in the group of animals irradiated by neutrons (fig. 12). In mice subjected to gamma rays, as in the control animals, the fluctuations of the number of erythrocytes did not exceed the limits of natural variability.

Summary data on the analysis of the morphological composition of the blood for four series of experiments, including this series, were processed using

the Wilcoxon's method of nonparametric statistics. The differences between changes of the investigated morphological indices in groups subjected to neutron and gamma irradiations combining the results of the four series of experiments were reliable. These data were presented in detail in the first communication. The use of the "t" test for processing the data of this series did not make it possible to detect statistical reliability between changes of the morphological indices of the irradiated groups.

Conclusions

1. Acute whole-body irradiation by neutrons (25 rad) caused more significant changes in the motor drinking reflexes of mice than gamma irradiation in the same dose.

2. In mice irradiated by neutrons the stimulation processes were attenuated to a greater degree than in mice subjected to gamma irradiation. In the first, the latent period of the conditioned reflex increased more sharply and there were more frequent cases lacking conditioned reflexes and disruptions of the proper force relationships. In mice subjected to gamma irradiations, the increase of the latent period of the conditioned reflex, some decrease of the running rate, and increase of the number of cases lacking a conditioned reflex were replaced in the second 10-day period after irradiation by improvement of these indices, compared to the initial background. In mice irradiated by neutrons, phases of improvement of some indices of higher nervous activity were not /164 observed. It was possible to detect only some small decrease of the number of cases rejecting water.

3. After gamma irradiation there was disinhibition of differentiation in mice while after neutron irradiation according to some indices, intensification of differentiations. However, the more complex criterion indicated a defective character of active inhibition in this group as well. Intensification of differentiation after neutron irradiation is attributed to summation of conditioned and protective inhibition. The latter was expressed most sharply in this group of animals.

4. A parallelism is noted between the dependence of disruptions of conditioned reflex activity on linear ionization density and changes of the hematological indices.

CHARACTERISTICS OF EFFECT OF DIFFERENT TYPES OF RADIATION
ON THE HIGHER NERVOUS ACTIVITY OF SMALL ANIMALS

A. P. Korolevskiy

ABSTRACT

A study was made of the comparative effect of fast neutrons, and 510 MeV protons and gamma radiations in doses of 150 rad on the higher nervous activity of "August" rats. The motor drinking conditioned reflex method was used. Disturbances of excitation and inhibition processes were detected in all irradiated animals. Neutron and gamma irradiations resulted in greatest disruption of the excitation process, whereas proton irradiation caused greatest disruption of the inhibition process. Neutron irradiation was most effective, while proton irradiation was least effective.

Comparative Effect of Fast Neutrons, Protons and Gamma
Radiations in a Dose of 150 rad (Communication III)

This communication is part of a series of studies devoted to investigating the comparative effect of neutrons, gamma rays and protons on the higher nervous activity of mice and rats. /165

The results of experiments on the comparative effect of neutron, proton and gamma irradiations in a dose of 300 rad and neutron and gamma radiations in a dose of 25 rad are published in our earlier articles in this collection. Summary data for all series of experiments on mice and rats were published earlier (N. N. Livshits, A. P. Korolevskiy).

Information on the reliability of the results is given in the summary article and also in articles devoted to individual series of experiments.

This report describes the results of investigation of the comparative effect exerted on higher nervous activity of rats by fast neutrons, protons and gamma radiations in a dose of 150 rad.

In this investigation, as in the experiments on mice, we employed the conditioned reflex motor method with drinking refreshment. The application of the stimuli and the recording of the principal indices of the conditioned

reflex reaction were done by an automatic apparatus designed by us. The animal reacted to the conditioned stimulus by running from a box to the place of refreshment along a groove inclined 35° to the horizon. The conditioned reflex stereotype consisted of positive conditioned stimuli (sound and light) and a differentiated sound stimulus.

The characteristics of the conditioned reflex activity of each animal ^{/166} were compiled on the basis of 20 experiments, set up after firmly establishing the stereotype. The same number of tests was also run after exposure to radiation. The experiments were made using "August" rats, mature males weighing 150-180 g. Prior to irradiation the rats were divided into four groups in such a way that each of the animals in any of the groups had a partner with similar indices of conditioned reflex activity in each of the remaining groups. Thus, the makeup of the groups, insofar as possible, was identical with respect to the indices of higher nervous activity. The indices of the conditioned reflex activity of animals subjected to irradiation were compared with the indices of the background conditioned reflex activity of these same animals and the animals of the control group.

The experimental animals were subjected to acute whole-body irradiation. The physical characteristics of irradiation are given in table 1.

TABLE 1. PHYSICAL CHARACTERISTICS OF RADIATION (150 rad).

Group	Type of radiation	Dose, rad	Dose intensity, rad/hr
a	Co ⁶⁰ gamma radiation	150.0	1230.0
b	1.25 MeV neutrons + gamma radiation	107.0 + 42.0	236.0
c	510 MeV protons	150	3348.0

The fourth group was not irradiated and served as control.

In the statistical processing of the data the mean values of each index in any group of animals were determined on the basis of experimental data obtained from 5 animals during the course of 10 experiments.

The changes of the indices of conditioned reflex activity in the groups of animals subjected to irradiation for the most part were similar in their direction to the changes already described in preceding studies¹ and only differed

¹See Communications I and II in this collection.

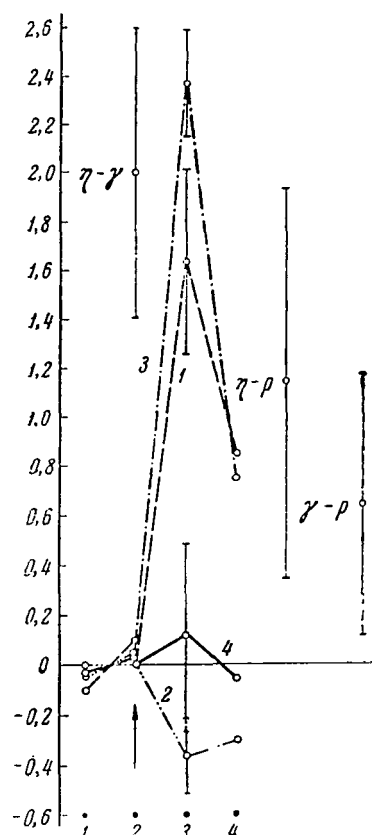


Figure 1. Mean changes of latent period of conditioned reflex after exposure to neutron, proton and gamma radiations (150 rad).

Along x-axis -- time (1 graduation = 10 experimental days). Along y-axis -- absolute mean value of deviation from initial mean level (sec). Day of exposure denoted by arrow. Vertical lines on curves denote errors of mean values. 1, Gamma; 2, protons; 3, neutrons; 4, control.

quantitatively, which was related to the change of the dose of irradiation and the species characteristics of the animals.

Change of the latent period of the positive conditioned reflex, running speed in response to the conditioned stimulus (intensity of the conditioned reflex) and the duration of the drinking reaction in the groups of animals irradiated by neutrons and gamma rays indicated a sharp attenuation of the stimulating process. In comparison with the mean initial background, the latent period of the reflex was lengthened considerably in both groups, and the intensity of the reflex (running rate) and duration of the animal's stay at the drinking bowl decreased (figs. 1, 2 and 3). /167

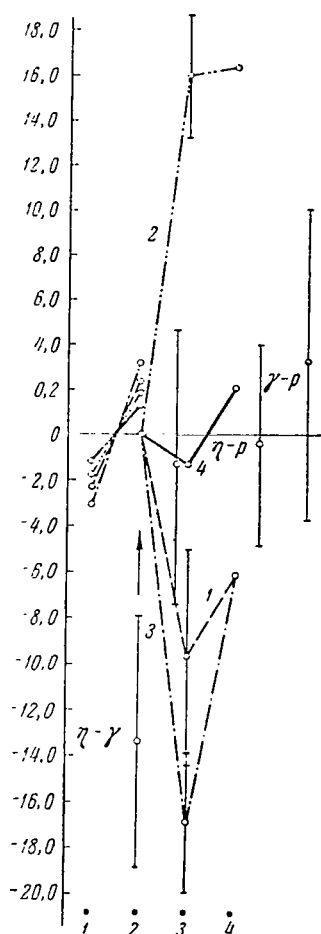


Figure 2. Mean changes of intensity of conditioned reflex after exposure to neutron, proton and gamma radiations (150 rad). Along y-axis -- absolute mean value of deviation from mean initial level (cm/sec). Other notations same as in fig. 1.

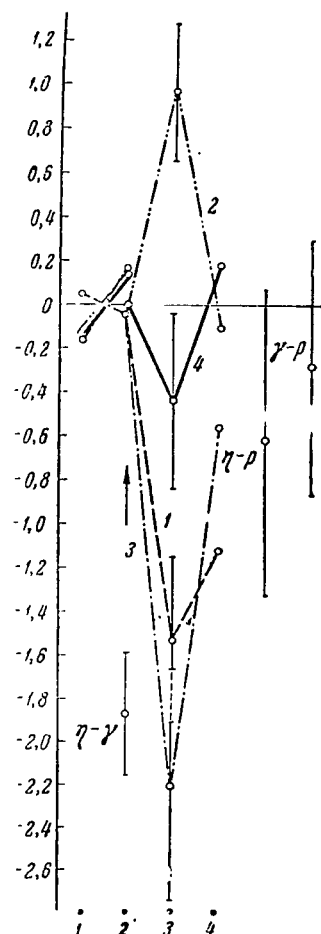


Figure 3. Mean changes of duration of drinking reaction to conditioned stimulus after exposure to neutron, proton and gamma radiations (150 rad). Notations same as in fig. 1.

In the animals irradiated by neutrons the changes of the latent period, the intensities of the conditioned reflexes and the durations of the stay at the drinking bowl were more clearly expressed than in animals subjected to gamma irradiation. In animals irradiated by protons the latent period of the reflex, intensity of the reflex and duration of the drinking reaction changed in a direction opposite to that described. The mean latent period in this group of animals decreased by almost 0.4 sec in comparison with the mean value of the initial level, and the intensity of the reflex increased still more significantly (figs. 1 and 2). The time of the drinking reaction after

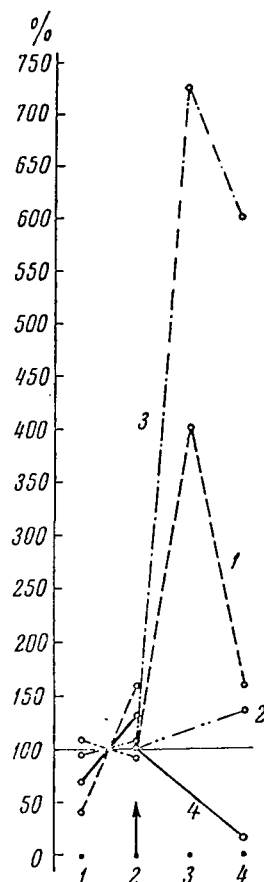


Figure 4. Changes of number of extinctions of conditioned reflex after exposure to neutron, proton and gamma radiations (150 rad). Along y-axis -- number of extinctions of conditioned reflexes in percent of mean initial level. Other notations same as in fig. 1.

application of the conditioned stimulus in the first 10-day period also increased sharply (fig. 3). In the control group at this same time the values of the latent period and the intensities of the conditioned reflex did not exceed the limits of their fluctuations at the norm. The time of the drinking reaction in this group of animals decreased somewhat.

The number of extinctions of the conditioned reflex in the group of animals irradiated by neutrons and gamma rays increased considerably in the course of the first 10-day period after exposure, which also indicates attenuation of the stimulation process (fig. 4). In the group of animals irradiated by neutrons the increase of the number of extinctions of the conditioned reflex at

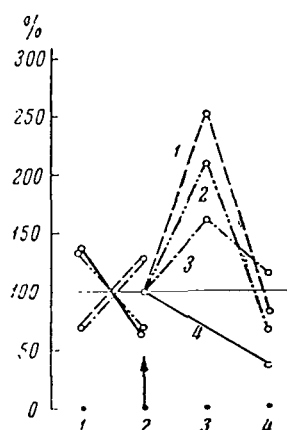


Figure 5. Changes of numbers of rejections of water after exposure to neutron, proton and gamma radiations (150 rad).

Along y-axis -- number of rejections of water in percent of mean initial level. Other notations same as in fig. 1.

this time exceeded almost by twice the number of extinctions in the group subjected to gamma irradiation.

In the animals subjected to irradiation by protons the change of the number of extinctions of the conditioned reflex was insignificant and unreliable.

In the control group the number of extinctions of the conditioned reflex decreased. It can be surmised that this is the result of conditioning, which in the irradiated animals disrupted the damaging effect of irradiation.

The number of cases of rejection of drinking refreshment increased in all groups of animals subjected to irradiation. However, in contrast to the preceding index, the number of rejections of water in the group exposed to gamma irradiation exceeded the number of rejections in the groups irradiated by protons and neutrons (fig. 5).

In the animals subjected to neutron irradiation the number of rejections of refreshment in the course of the first 10-day period, in comparison with the remaining irradiated groups of animals, was the lowest.

Thus, in the groups of animals subjected to irradiation by neutrons and gamma rays in a dose of 150 rad, there was a characteristic noncorrespondence in the changes between the two latter indices.

The absence of correlation between the changes of two indices of the state of the stimulation process, close in value, was also observed in the case of

irradiation of mice by neutrons and gamma rays in doses of 25 and 300 rad. /170
 In one of our studies we proposed the following possible explanation of the absence of such a correlation: extinction of the conditioned motor reflex is an index of a severer disruption of the stimulating process than inhibition only in the last link of the reflex -- reaction to drinking. Therefore, in the group of animals in which the stimulating process suffered more severely, the first of these disruptions was observed more frequently, while in the group irradiated by gamma rays the second disruption was observed more frequently. It should also be added that with exposure to a dose of 150 rad, the absence of correlation between the number of extinctions of conditioned reflexes and the number of rejections of refreshment was also observed in relationships of the values of the changes of these indices in the groups of rats irradiated by neutrons and protons.

The latter was absent in the case of exposure of mice to a dose of 300 rad.

In the animals of the control group the number of rejections of drinking refreshment, like the number of extinctions of the conditioned reflex, decreased in the course of the first 10-day period and also continued to decrease in the second 10-day period after irradiation.

We took into account phase phenomena for the latent period of the /171
 conditioned reflex. In contrast to the earlier experiments on mice irradiated in doses of 300 and 25 rad, in these experiments the number of paradoxical phases after irradiation did not increase, but instead decreased. A decrease of the number of paradoxical phases was observed in the control animals as well (fig. 6). Apparently conditioning of the stimulation process was present in this period in all groups of rats.

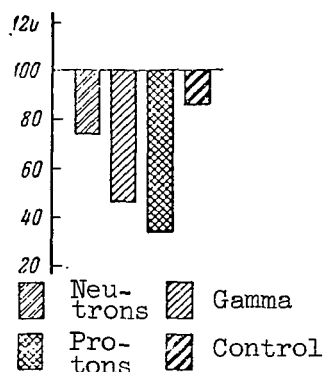


Figure 6. Changes of number of paradoxical phases after exposure to neutron, proton and gamma radiations (150 rad). Along y-axis -- number of paradoxical phases in percent of mean initial level.

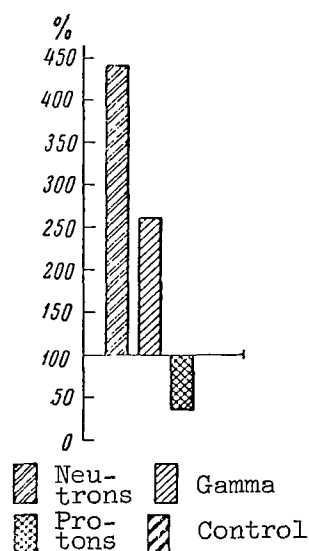


Figure 7. Changes of number of adjustment phases after exposure to neutron, proton and gamma radiations (150 rad).
Along y-axis -- number of adjustment phases in percent of mean initial level.

The number of adjustment phases, according to this index, increased in the rats irradiated by neutrons, both in comparison with the initial level and in comparison with the control and the remaining irradiated groups. After exposure to gamma rays, the increase of the number of adjustment phases was less clearly expressed. In the group irradiated by protons the number of adjustment phases decreased in comparison with the initial background and the control animals (fig. 7).

After irradiation, in all groups of animals, including the controls, differentiation intensified, which was related to conditioning; however, in rats irradiated by protons the conditioning process lagged considerably behind conditioning in the control group, which is evidence of attenuation of conditioned inhibition (figs. 8, 9 and 10). In the rats subjected to gamma irradiation the differentiation for the latent period was the same, but for the rate of running it was more clearly expressed than for rats irradiated by protons, but weaker than for the control group. This group almost did not differ from the control group with respect to the duration of the drinking reaction to differentiation after running. Thus, in comparison with the control group, the inhibition process suffered in rats subjected to proton and gamma irradiation.

Somewhat different relationships were noted in rats irradiated by neutrons. In this group of animals the latent period of the reaction to differentiation in the first 10-day period was longer than in the control rats, and in the second 10-day period almost did not differ from this index for

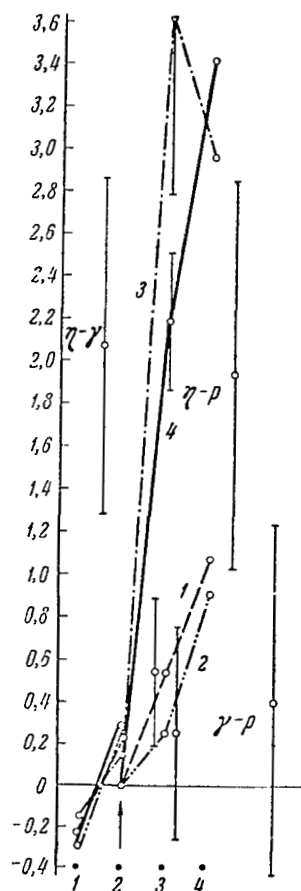


Figure 8. Mean changes of latent period of relative differentiation after exposure to neutron, proton and gamma radiations (150 rad). Notations same as in fig. 1.

the control group. The rate of running in response to the differentiated stimulus was equal to the same index for the control rats. In rats irradiated by neutrons the duration of the drinking reaction was maximum. It considerably exceeded the value of this index both for the control rats and for rats subjected to exposure to protons and gamma rays.

In our earlier studies,¹ in a discussion of the effect of neutrons, protons and gamma rays in doses of 300 and 25 rad on the conditioned inhibition of mice, we postulated that improvement of the indices of conditioned inhibition in mice irradiated by neutrons is the result of a summation of conditioned and

¹See article by this same author in this collection.

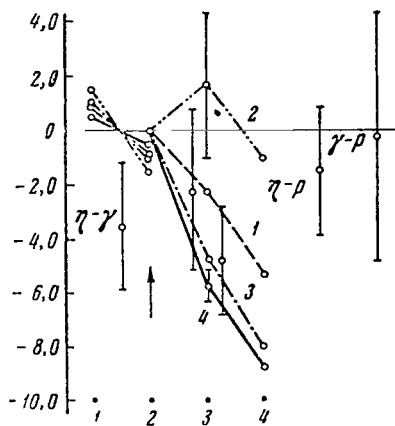


Figure 9. Mean changes of running rate in response to differentiated stimulus after exposure to neutron, proton and gamma radiations (150 rad). Along y-axis -- absolute mean value of deviation from initial mean level (cm/sec). Other notations same as in fig. 1.

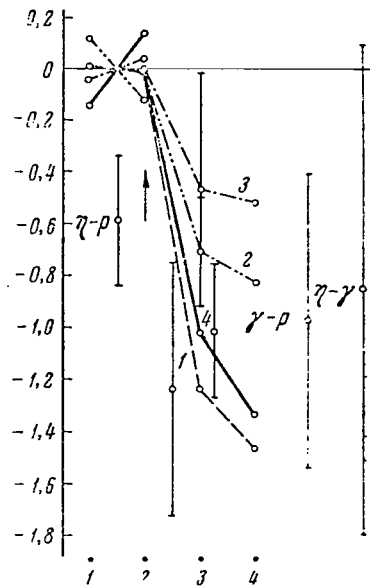


Figure 10. Mean changes of duration of drinking reaction to differentiated stimulus after exposure to neutron, proton and gamma radiations (150 rad). Notations same as in fig. 1.

protective inhibitions. The importance of this mechanism in the reactions of the higher parts of the central nervous system to irradiation already has been pointed out in the literature.

It can be postulated that some shortening of the latent period of the reaction to differentiation in the second 10-day period in the group of rats irradiated by neutrons occurred due to attenuation of protective inhibition, that is, it was the result of restoration of the function. At the same time, some intensification of the differentiated reaction in the groups of animals subjected to proton and gamma irradiations occurred due to intensification of inhibition as a result of functional restoration and under the influence of conditioning.

In the last groups of animals, in the course of the second 10-day period, conditioning did not have the effect observed in the control group because of attenuation of the inhibition process. We assume that the intensification of differentiation for the latent period and its persistence by virtue of the conditioned reflex in animals irradiated by neutrons is the result of a summation of conditioned and protective inhibitions. It should be noted that in this series of experiments on rats the protective inhibition was less effective.

The less significant expression of protective inhibition in this series of experiments is also confirmed by the fact that in this case the change of the number of phase phenomena was less clear. In rats subjected to neutron irradiation there was a reliable increase only in the number of adjustment phases. The number of paradoxical phases decreased in this group even to a somewhat greater extent than in the control animals. The latter, however, was not statistically reliable.

Somewhat different relationships were noted in changes of the index of the drinking reaction after running in response to the differentiated stimulus. In this series of experiments the changes of this index in rats irradiated by neutrons resemble the effects of irradiation in a dose of 25 rad /174 in experiments on mice. It was found that extinction of the last link of the reaction to the differentiated stimulus, intensified by additional progressively positive stimuli of the drinking bowl situation was a difficult problem. In actuality, in the control group in the course of the first 10-day period after irradiation of the experimental groups, the duration of the drinking reaction decreased by a factor of almost six and continued to decrease in the second 10-day period as well.

Similar phenomena were observed in rats subjected to gamma irradiation. In the remaining two groups of irradiated rats this function was less susceptible to conditioning; this capability also suffered most severely in this case in animals irradiated by neutrons.

The change of the reaction to differentiation in the irradiated groups of rats, in our opinion, should be considered the result of two processes: attenuation of conditioned inhibition and the summation of protective and conditioned inhibitions.

As demonstrated above, in rats irradiated by protons the phenomena of protective inhibition were not clearly expressed, and with respect to all indices there was only a disinhibition of differentiation. In rats irradiated by neutrons the protective inhibition was clearly expressed. Therefore, with respect to indices not requiring stresses of the inhibition process (latent period of the reaction and rate of running in response to differentiation), the differentiations either were not worse or even were better than in the control animals, because in these cases the effect of summation of the protective and conditioned inhibitions occurred. However, with respect to an index requiring considerable stress of the inhibition process (duration of the drinking reaction after running in response to differentiation), the inadequacy of the inhibition process was manifested so strongly that the summation of the protective and conditioned inhibitions could not compensate it.

In rats subjected to gamma irradiation the attenuation of inhibition processes was manifested by a decrease of the latent period and an increase of the intensity of the reaction to an unreinforced stimulus and the duration of the stay at the drinking bowl was the same as in the control group. We already had encountered this phenomenon in an investigation of the effect of gamma and

proton irradiation in a dose of 300 rad.¹ As mentioned above, we cannot now indicate the specific mechanisms of this phenomenon, but we assume that the changes of differentiation are related to the effect of attenuation of both stimulation and inhibition processes. These factors can be combined in different ways.

The disruption of conditioned inhibition in rats irradiated by protons was most clearly expressed. We therefore assume that the decrease of the /175 latent period of the conditioned reflex and the increase of the running rate in these animals in response to the conditioned stimulus was not the result of intensification of a stimulating process, but due to considerable attenuation of inhibition. In particular, there was a disruption of the most sensitive inhibition process, which was manifested in a disinhibition of differentiations, and the increase of the conditioned reflex obviously occurred secondarily, not as a result of intensification of the excitation process, but due to attenuation of the inhibition process, and therefore due to disruption of the intensity balance between these two nervous processes. The fact that the excitation process in this group was attenuated rather than intensified is indicated by the considerable increase of the number of cases of rejection of

During neutron irradiation the inhibition process also attenuated. At the same time there was attenuation of the excitation process (decrease of conditioned reflexes, expressed in an increase of the latent period, decrease of intensity of the reflex, etc.). However, in these animals the quite substantially expressed protective inhibition and its summation with unconditioned inhibition masked attenuation of conditioned inhibition. The latter can be detected only when using the most difficult criterion, requiring stresses of the inhibition process, which we mentioned above. Thus, investigation of the effect of fast neutrons, protons and gamma rays on the higher nervous activity of "August" rats in a dose of 150 rad revealed that the effectiveness of the administration of different types of radiations is different, but with respect to the main indices of conditioned reflex activity is directly proportional to the linear ionization density. The effect of neutrons caused a maximum disruption of the functions of the CNS. Gamma rays caused relatively fewer disruptions. According to most indices the effects of proton irradiation differed from the effect of the other two types of irradiation both quantitatively and qualitatively. Only with respect to some indices of conditioned reflex activity was the effectiveness of exposure to protons close to the effectiveness of exposure to gamma rays (latent period of the differentiated reaction). According to other indices (latent period and intensity of the conditioned reflex, duration of the drinking reaction, etc.), exposure to protons caused an effect opposite of exposure to neutrons and gamma rays. Finally, according to some indices (the number of extinctions of the conditioned reflex) the effectiveness of exposure to protons was insignificant. This circumstance shows that in functional respects the exposure to different types of radiation can be manifested differently in different indices of conditioned reflex activity.

Table 2 gives the results of statistical processing of the experimental data, using Student's test.

¹ See article in this collection.

TABLE 2. PROBABILITY OF RANDOM DISCREPANCIES OF MEAN VALUES
(STUDENT'S TEST) (150 rad).

Index of conditioned reflex activity	Compared types of radiations	Probability of random discrepancy (P)
Latent period of conditioned reflex	n-γ	P > 0.05
	p-γ	P > 0.05
	n-p	P < 0.01
Intensity of conditioned reflex	n-γ	P > 0.05
	p-γ	P < 0.05
	n-p	P < 0.05
Drinking reaction to condi- tioned reflex	n-γ	P > 0.05
	p-γ	P > 0.05
	n-p	P < 0.05
Latent period of differen- tiated reaction	n-γ	P > 0.05
	p-γ	P > 0.05
	n-p	P > 0.05
Intensity of differentiated reaction	n-γ	P > 0.05
	p-γ	P > 0.05
	n-p	P > 0.05
Drinking reaction to differen- tiation	n-γ	P > 0.05
	p-γ	P > 0.05
	n-p	P > 0.05
No. of cases of absent conditioned reflex	n-γ	P < 0.05
	p-γ	P > 0.05
	n-p	P < 0.05
No. of cases of refusal to drink	n-γ	P > 0.05
	p-γ	P > 0.05
	n-p	P > 0.05
No. of paradoxical phases (for duration of latent period of conditioned reflex)	n-γ	P > 0.05
	p-γ	P > 0.05
	n-p	P > 0.05
No. of adjustment phases (for this same index)	n-γ	P > 0.05
	p-γ	P > 0.05
	n-p	P < 0.05

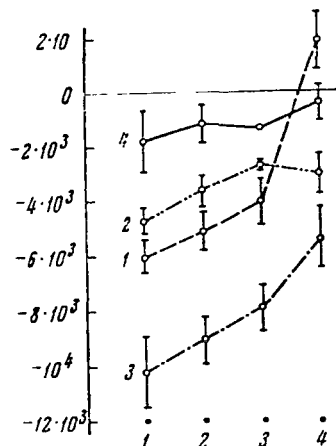


Figure 11. Dynamics of changes of content of leukocytes in the peripheral blood after exposure to neutron, proton and gamma radiations (150 rad). Along x-axis -- time in weeks. Along y-axis -- absolute mean deviation of number of cells from mean initial level. Vertical lines on curves represent errors of mean values. Other notations same as in fig. 1.

Results of analysis of the reliability of the differences in the effectiveness of the three types of radiation on the basis of summary data for the four series of experiments, using the nonparametric statistics method, are given in our first communication. We recall here only that the differences of the changes in the groups subjected to neutron and gamma irradiation were reliable on the basis of the summary data for the latent period of the conditioned reflex, latent period of the relative differentiated reaction and duration of the drinking reaction to a differentiated stimulus. The differences between the groups of animals after proton and gamma irradiations were reliable for the latent period of the conditioned reflex, intensity of the reflex and the latent period of the relative differentiated reaction. /176

Analysis of the morphological composition of the blood, as in our earlier studies, revealed that the changes of the hematological indices correlated with the changes of conditioned reflex activity. In rats irradiated by neutrons leukopenia was expressed considerably more sharply than in the other irradiated groups of animals (fig. 11). A decrease of the number of leukocytes by more than 10,000 cells from the mean value of the initial level was discovered the day after irradiation. /177

The number of leukocytes gradually was restored from sample to sample, but by the end of the observation period was almost 5,500 cells less than the

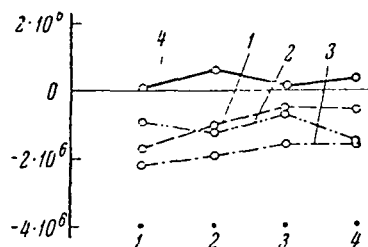


Figure 12. Dynamics of changes of content of erythrocytes in peripheral blood after exposure to neutron, proton and gamma radiations (150 rad). Notations same as in fig. 11.

initial value. In the group of animals subjected to gamma irradiation the number of leukocytes decreased to a lesser degree (by 6,000 cells from the mean value of the initial level). Up to the third sample the processes of restoration of the number of leukocytes occurred concurrently in this group of animals and in the group irradiated by neutrons. However, by the fourth sample the number of leukocytes in the group of animals subjected to gamma irradiation was restored to the initial level, passing into a slight leukocytosis, whereas in the group of animals irradiated by neutrons the restoration was far from complete. In the group of animals irradiated by protons, in which there was a decrease of 5,000 cells, the number of leukocytes was restored by the third sample to a difference of 3,000 cells from the initial level (with an increase by 1,000 cells from sample to sample), parallel with the process of restoration in the animals irradiated by gamma rays. By the fourth sample the number of leukocytes again began to decrease. In the control group the number of leukocytes decreased by 2,000 cells in the first sample, which does not exceed the fluctuations of the norm in rodents, and was gradually restored to the initial level.

The decrease of the number of erythrocytes occurred to a considerably ^[178] lesser degree in the irradiated group of animals and revealed the same dependence on linear ionization density as the decrease of leukocytes (fig. 12). The results of statistical analysis of data on the differences in the composition of the peripheral blood at different stages of observations among the groups of animals irradiated by the three types of radiation, using Student's test, are given in table 3.

Summary data on investigation of the composition of the peripheral blood for four series of experiments, including this series, were analyzed using Wilcoxon's test. The results of the analysis were given in our first communication.¹

¹See first article by this same author in this collection.

TABLE 3. PROBABILITY OF RANDOM DISCREPANCIES OF MEAN VALUES OF CONTENT OF LEUKOCYTES AND ERYTHROCYTES IN PERIPHERAL BLOOD (ANALYZED WITH STUDENT'S TEST) (FOURTH SERIES OF EXPERIMENTS -- 150 rad).

Type of radiation	Leukocytes (samples)				Erythrocytes (samples)			
	I	II	III	IV	I	II	III	IV
n-γ	P>0.05	P>0.01	P>0.05	P>0.01	P>0.05	P>0.05	P<0.05	P>0.05
p-γ	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05
n-p	P>0.05	P<0.05	P<0.05	P>0.05	P<0.05	P>0.05	P>0.05	P>0.05

In the control group the change of the number of erythrocytes, like the number of leukocytes, did not exceed the limits of their natural variation.

Conclusions

1. Acute whole-body irradiation of "August" rats in a dose of 150 rad by fast neutrons, 510 MeV protons and gamma rays caused dissimilar changes in the motor drinking reflexes of rats; exposure to neutrons revealed a maximum effect and irradiation by protons produced a minimum effect. The exposure to gamma radiation occupied an intermediate position between the effect of protons and neutrons.

2. Excitation processes in rats irradiated by neutrons suffered more severely than in rats exposed to gamma irradiation. The latent period in animals irradiated by neutrons increased more steeply and cases of absence of conditioned reflexes were more frequent. Disruptions of force relationships in the animals of this group were more frequent than in the animals of the remaining groups. The effect of gamma rays was generally similar to the effects of exposure to neutrons, but the degree of changes was expressed more weakly than /179 in the case of irradiation by neutrons. The effect of protons led to a relative intensification of the excitation process according to most of the indices.

3. After irradiation by neutrons there was a deepening of differentiation for the part of the indices of differentiated reaction unrelated to stress of the inhibition process, caused by summation of protective and conditioned inhibitions. The effect of gamma radiation led to disinhibition of differentiation, according to some indices. After irradiation by protons the differentiations were disinhibited with respect to all investigated indices. According to the difficult criterion, requiring a great stress of the inhibition process (duration of the drinking reaction) among the rats irradiated by neutrons, the differentiations were disinhibited more sharply than in the animals irradiated by protons.

4. The effect of neutrons, gamma rays and protons causes disruptions of both excitation and inhibition processes. As a result of neutron and gamma ray irradiations, the most serious disruptions are inflicted on the excitation process, while irradiation by protons causes greatest disruption of the inhibition process.

5. There is a parallelism between the dependence of the disruptions of conditioned reflex activity on linear ionization density and changes of hematological indices.

COMPARISON OF THE EFFECT OF WHOLE-BODY CHRONIC AND ACUTE
GAMMA IRRADIATION ON THE HIGHER NERVOUS ACTIVITY
OF WHITE RATS (THE ROLE OF THE TIME FACTOR)

Ye. S. Meyzerov

ABSTRACT

Two groups of rats were exposed to whole-body gamma irradiation by Co^{60} in a dose of 160 hr. One group was irradiated at a dose rate of 85 r/min and the other at the rate of 6 r/day.

The conditioned motor alimentary reflexes and the cell content of the peripheral blood were studied in the rats.

Acute and chronic irradiations caused similar changes in the conditioned reflexes. According to some data, the disturbances of higher nervous activity were somewhat more severe in rats exposed to chronic irradiation. The difference between the changes in these indices in the irradiated groups was not large, but nonetheless these changes were statistically reliable.

Contrary to the reactions of higher nervous activity, the decrease of leukocyte, erythrocyte and hemoglobin content in the peripheral blood was more sharply expressed in animals exposed to acute irradiation.

The investigation of the role of the time factor in the reactions of 180 the CNS to irradiation is of great importance for understanding the mechanism of radiation reactions observed in hygiene work and space biology, because when using nuclear energy on the ground and in space flights there can be a different distribution of radiation doses with time.

A great many investigations have been devoted to the effect of ionizing radiations on the CNS; these have been reviewed in monographs by A. V. Lebedinskiy and Z. N. Nakhil'nitskaya (1960); N. N. Livshits (1961); M. N. Livanova (1962); P. F. Minayeva (1962) and I. A. Piontkovskiy (1964). We have not succeeded in finding even one specialized experimental study in the available literature which deals with the role of the time factor in the effect of irradiations on the conditioned reflexes. Investigation of this problem was the object of our study.

Method

The work was done using the L. I. Kotlyarevskiy motor-alimentary method in a modernized chamber, using Wistar male rats weighing 160-180 g at the time the investigations began. The experiments were carried out using the following stereotype (table 1). The intervals between administrations of the stimuli varied from 75 to 150 sec, depending on the position of the rat in the chamber: the stimulus was applied only at the time when a rat was seated with his head toward the food tray. The investigations of higher nervous activity were accompanied by observations of the peripheral blood, weight and general condition of the animals.

TABLE 1. EXPERIMENTAL CONDITIONS.

Conditioned stimulus	Time of general effect of conditioned stimulus, sec	Time of isolated effect of conditioned stimulus, sec
Tone 1-800 cps (level of sound intensity 35 db)	10	5
Red light (lighting of 8-W lamp)	10	5
Red light (lighting of 8-W lamp)	10	5
Tone 1-800 cps (level of sound intensity 35 db)	10	5
Tone 2-400 cps -- differ- entiation (level of sound intensity 30 db)	10	-
Tone 1-800 cps (level of sound intensity 35 db)	10	5
Red light (lighting of 8-W lamp)	10	5
Tone 1-800 cps (level of sound intensity 35 db)	10	5

Hematological indices were investigated on a special group of rats subjected to irradiation under identical conditions. This was done in order /181 to exclude the influence of even an insignificant trauma during the removal of the blood on the conditioned reflex activity.

The characteristics of the conditioned reflex activity of each animal were determined on the basis of the results of 45-50 experiments carried out after establishment of the stereotype, which was necessary for obtaining sufficient material for statistical analysis.

In order to clarify the typological characteristics, the rats were subjected to the following tests: lengthening of differentiation to 3 min, daily starvation, injection of caffeine, effect of unconditioned inhibition and physical load prior to the experiment.

After formulating and establishing the stereotype, the investigations of variations of the conditioned reflex background and determination of the typological characteristics of the animals, they were subjected to irradiation. By this time the rats weighed 260-280 g.

Irradiation Conditions. Chronic irradiation was accomplished on an apparatus which we created and in a special box; dosimetric measurements were made

regularly by dosimetric engineer M. M. Korotkov. The source was a Co^{60} point source with an activity of 125 mCi. The cage with the animals was placed under the source, 80 cm from it. The dose intensity was 0.276 r/hour; the uniformity of the irradiation field was ± 5 percent. The rats were irradiated daily for 22 hours a day; the daily dose was 6.07 r. Acute radiation was accomplished using a GUBE-800 apparatus with a dose intensity of 85 r/min, singly in a dose /182 of 160 r; the duration of the irradiation was not much less than 2 min.

The rats were subjected to chronic irradiation daily, except Sundays, until a total dose of 160 r had been administered. After the irradiation had been completed the animals were observed for 100 days.

Neither the chronic nor the acute irradiations caused significant changes in the weight of the animals. The rats remained in good spirits and active during the irradiations and after their completion and continued to eat the food given them. Their sanitary reflexes were normal, which was confirmed by the condition of their coats. During the entire period of the work the coats were smooth and shiny. The irradiation of the rats caused a decrease of the total number of leukocytes, erythrocytes and the hemoglobin content in the peripheral blood.

Research Results

Chronic Irradiations¹

In the study of the results of the experiments for individual rats we found both certain differences and features in common. The dynamics of the changes of the higher nervous activity at the time of chronic irradiations and in the course of the first two periods of the aftereffect in all 11 rats were the same. On the very first days of irradiation, after administration of a

¹The results of this series of experiments (Ye. S. Meyzerov) on part of the animals were published by us earlier. Here we will mention these data briefly, because this is necessary for comparison with the effect of acute irradiations.

dose of 6-12 r, all rats manifested onset of a phase of initial deterioration of higher nervous activity. This phase was characterized not only by a decrease of the values of the positive conditioned reflexes, but also by disruption of the correct force relationships in the form of adjustment phases, and in some of the animals also paradoxical phases, in most cases at the intermediate and low levels. Thereafter, despite the fact that the irradiations continued and the dose increased, a phase of relative improvement of the conditioned reflex background appeared, which approached the initial level, but in most cases did not entirely reach this level. After administration of 54-72 r there was a second wave of disruption of higher nervous activity, more severe and intense than in the first period; the decrease of the conditioned reflexes was more significant, paradoxical phases at the low and intermediate levels were observed in all animals, and there were cases of extinction of artificial, and in some animals, also the natural conditioned reflexes. Differentiated inhibition was weakened in this period in all rats. In the 30-40 days after the end of irradiation there was further deterioration of the higher nervous activity, and only upon completion of this period did the conditioned reflex activity begin to improve. The initial level of higher nervous activity was attained in all but one of the rats (No. 6), observations of which were interrupted due to pneumonia and death of the animal. It is obvious that the illness prevented the full normalization of higher nervous activity in this rat. In three rats (Nos. 12, 2 and 18) the initial level of higher nervous activity was completely restored by the end of the observation period. In seven rats (Nos. 4, 8, 10, 14, 16, 20 and 22) conditioned reflex activity during this period was better, according to a number of indices, than prior to irradiations. /183

Our experimental data were inadequate for determining the correlation between the type of higher nervous activity and its impairments caused by irradiations, but some characteristics of the reactions to irradiation, nevertheless, should be noted. The reaction of the higher parts of the brain to irradiation in rats of weak and intermediate types of nervous system was more severe than in animals of the strong type. The disappearance of unconditioned alimentary reflexes was observed only in three rats with weak and intermediate types of nervous system. The improvement of conditioned reflex activity in comparison with the initial level was observed only in animals with a strong (adjusted and unadjusted) type of nervous system and was absent in animals with weak and intermediate types of nervous system.

Acute Irradiations

V. B. Rozen (1960) describes the results of acute irradiations of rats in doses closest to those used in our study (150 r and 450 r).

However, for a quantitative comparison of the effect of acute and chronic irradiations on higher nervous activity the data in the literature could not be used. It was necessary to investigate the effect of acute irradiations on the functions with which we were concerned with rigorous adherence to the other experimental conditions. This was the objective of our experiments.

After acute irradiation with a dose of 160 r clearly expressed changes of conditioned reflex activity were observed in most of the rats on the fifth day after exposure.

Only in one case (rat No. 1) was this phenomenon observed on the third day, and in another rat (rat No. 17) it was observed on the sixth day after irradiation.

Together with a decrease of the values and a lengthening of the latent periods of the conditioned reflexes, phase phenomena were observed which indicated the development of protective inhibition. In the animals in which disruptions of force relationships were observed prior to irradiation, after exposure they increased in frequency and became more intense. Whereas /184 prior to irradiation only adjustment phases were observed, afterwards their number increased and paradoxical phases also appeared (rats Nos. 1, 7 and others). Differentiations were disinhibited in only two animals, but the appearance or intensification of subsequent inhibition indicated a weakening of the inhibition process. This also was indicated by the increase of inter-signal reactions.

This period lasted from 20 to 35 days and was replaced by a gradual normalization of higher nervous activity, lasting 20-30 days. In some of the animals (rats Nos. 1, 3, 5, 11, 15) the initial level of higher nervous activity was completely restored in this period, but in three animals (rats Nos. 7, 9, 17) the restoration of higher nervous activity was noted later, 55-60 days after irradiation.

By this time in rats Nos. 1, 3, 5, 11 the values of the conditioned reflexes exceeded the initial level, with retention of differentiations and the normal results of functional tests. In the remaining three rats there was stable adherence to the normal level of higher nervous activity during this period.

All five rats in which the restoration of higher nervous activity was observed in the earlier periods, and in most of which there was a phase of increase of the initial level according to a number of indices, can be classed as having a strong adjusted type of higher nervous activity.

Among the three rats for which the initial level of higher nervous activity was restored later and for which increases of the initial level were not observed, one rat had a weak, one had an intermediate and one had an unadjusted type of nervous system.

Comparison of the Influence of Acute and Chronic Irradiations on the Higher Nervous Activity of Rats

It was pointed out before that the reactions to irradiation to a certain degree were related to the type of higher nervous activity of the animals. In order to be able to make a quantitative comparison of the results of acute and chronic irradiations, it was necessary to ensure an identical makeup of both

groups. Particular attention was given to this in the selection of the animals. The rats in which sharply expressed deviations of the indices of higher nervous activity from the mean level were noted were rejected prior to irradiation. However, we were not able to obtain a numerical equality of the groups, because some of the rats died of various illnesses (pneumonia, otitis).

We now present data on the makeup of the compared groups of rats with respect to type of higher nervous activity.

Group of rats	Strong adjusted	Strong unad- justed	Inter- mediate	Weak
Chronically irradiated	6	2	2	1
Acutely irradiated	5	1	1	1

It can be seen that most of the rats in each group had a strong ad- /185
justed type of higher nervous activity. However, in the group of chronically irradiated rats the animals of this type represented 54.5 percent of the total, whereas among the acutely irradiated rats it was 62.5 percent. In order to exclude the possible influence of this difference in some cases during the statistical processing of the data, we excluded three rats from the group of chronically irradiated animals. Thus the makeup of both groups became identical both qualitatively with respect to type of higher nervous activity, and numerically, as will be pointed out below.

Group of rats	Strong adjusted	Strong unad- justed	Inter- mediate	Weak
Chronically irradiated	5	1	1	1
Acutely irradiated	5	1	1	1

As mentioned above, the most characteristic aspect in the radiation reactions of the higher parts of the CNS of rats to irradiation was a decrease of the conditioned reflexes and disruption of proper intensity relations. Disinhibition of differentiations was less clearly expressed, but appeared regularly. These phenomena were observed in both irradiated groups. These data were processed statistically.

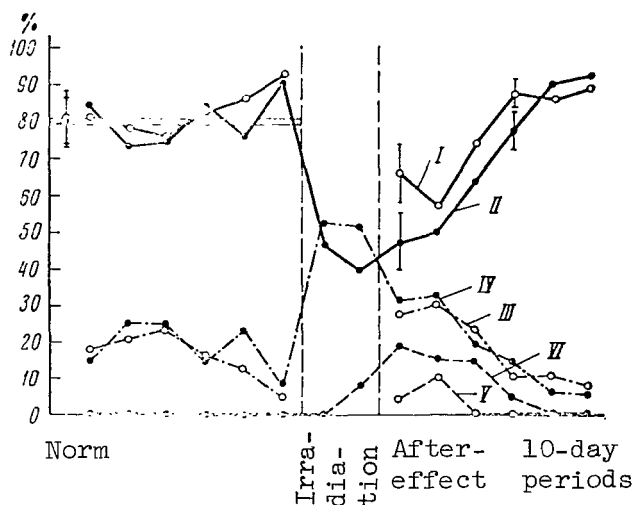


Figure 1. Effect of whole-body chronic and acute gamma irradiations on higher nervous activity of rats.

Time in 10-day periods is plotted along the x-axis. For acute irradiation: I -- experiments with normal higher nervous activity; III -- experiments with slight impairments of higher nervous activity; V -- experiments with severe impairments of higher nervous activity. For chronic irradiations: II -- experiments with normal higher nervous activity; IV -- experiments with slight impairments of higher nervous activity; VI -- experiments with severe impairments of higher nervous activity. Vertical dashed lines: left -- onset of chronic irradiations, right -- end of chronic irradiations and simultaneous end of acute radiation. Vertical lines on curves represent triple the mean error.

In the comparison of changes of values of positive conditioned reflexes in both groups we used Student's test, and for the other indices of conditioned reflex activity we used the alternative variability test. Phase phenomena, disinhibition of differentiations and cases of subsequent inhibition after differentiation were combined into the group of slight impairments of higher nervous activity, and cases of absent formed and unconditioned reflexes to reinforcement were assigned to the category of severe impairments of higher nervous activity.

Figure 1 shows data on impairments of higher nervous activity in both irradiated groups of rats. The illustration shows that there is a close similarity of the initial background in both groups with respect to the indices. The mean number of experiments without impairments of higher nervous activity, determined on the basis of data for 50 experiments on each of the rats, is 79-82 percent. The differences between the group means are far less

than the scatter of these values in each group. This confirms the correctness of selection of the groups.

The number of experiments with normal higher nervous activity decreases sharply at the time of chronic irradiation, but the number with slight impairments of higher nervous activity increases. Severe impairments of higher nervous activity also appear in the second 10-day period of irradiation. Their number increases after termination of the irradiations.

We will now compare the results of acute irradiations with the effect of chronic irradiations in the aftereffect, when the total radiation dose was fully administered. Figure 1 shows that after acute and chronic irradiations in the dynamics of the investigated indices there is a surprisingly close correspondence of a tendency to a more severe course of radiation reactions /187 in the chronically irradiated rats. The curves representing the changes of the number of experiments with normal higher nervous activity after irradiations in both groups run almost parallel to one another. The percentage of experiments with normal higher nervous activity is somewhat higher for animals subjected to acute irradiation. The difference is statistically reliable in the first and fourth groups of experiments after irradiations (each group includes experiments carried out on each group of rats for 15 days). Only in the fifth and sixth groups of experiments after irradiations was the percentage of experiments with normal higher nervous activity in the chronically irradiated rats somewhat higher than among rats subjected to acute irradiation, but this difference was statistically unreliable. The percentage of cases with severe impairments of higher nervous activity in the four groups of experiments after irradiations was somewhat greater among the chronically irradiated rats, but this difference is not so great, although statistically reliable.

In order to preclude the possibility of the slight nonuniformity of the makeup of the compared groups of animals exerting any influence on the differences in the reactions to irradiation, we excluded from the group of chronically irradiated animals three rats, thereby bringing about a full qualitative and quantitative uniformity of both groups, as mentioned above.

Figure 2 shows the results of statistical processing of the experimental data after equalization of the groups.

Figures 1 and 2 show that the exclusion of three rats from the group of chronically irradiated animals did not introduce any basic changes into the results of the statistical processing, and only slightly increased the statistical error in the group of chronically irradiated animals, which could be attributed to a decrease of the number of observations. This also confirms the correctness of the choice of the groups.

Conditioned inhibition was weakened in both groups. After irradiation there was an intensification of subsequent inhibition after differentiation and an increase of the number of intersignal reactions. The disinhibition of differentiations was more sharply expressed among the chronically irradiated rats, but the difference between groups was not statistically reliable. These data are shown in figure 3.

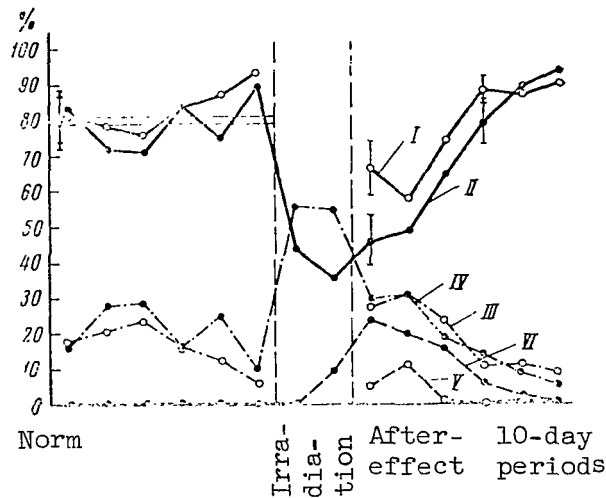


Figure 2. Effect of whole-body chronic and total acute gamma irradiations on higher nervous activity of rats.

Groups of rats subjected to acute and chronic irradiation were identical, qualitatively and quantitatively. Notations same as in fig. 1.

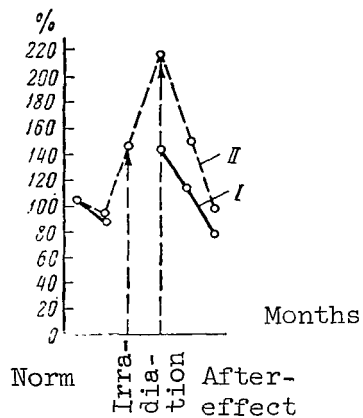


Figure 3. Effect of whole-body chronic and acute gamma irradiations on differentiated inhibition of rats.

Along x-axis -- time in months. Along y-axis -- number of disinhibited differentiations in percent in relation to initial level, assigned value 100 percent. I -- for acute irradiation; II -- for chronic irradiation. Arrows: left -- onset of chronic irradiations, right -- end of chronic irradiation and simultaneous end of acute irradiation.

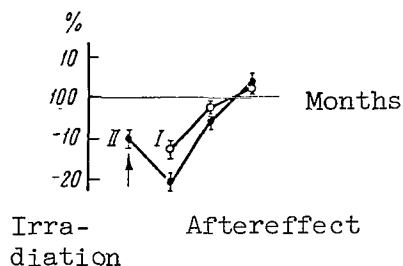


Figure 4. Effect of whole-body chronic and acute gamma irradiations on mean value of motor conditioned reflex of rats.

Along x-axis -- time in months. Along y-axis -- percentage deviation of value of conditioned reflex from mean value of norm, assigned value 100 %.

I -- for acute irradiation; II -- for chronic irradiation. Vertical lines on curves represent triple the mean error.

The decrease of the mean intensity of the conditioned reflex among the chronically irradiated rats was expressed to a somewhat greater extent than in the group subjected to acute irradiation. The difference between the groups was small, but statistically reliable (fig. 4).

In our earlier study (Livshits, Meyzerov, Apanasenko and Kuznetsova, 1962) we noted the somewhat severer impairments in the group of rats subjected to chronic irradiations in comparison with acutely irradiated rats. However, 188 on the basis of the data then at our disposal the difference was not statistically reliable and therefore we took care with the data then at hand. Then we formulated additional experiments, as a result of which we can now state with assurance that chronic irradiations cause more significant impairments of higher nervous activity than acute irradiations in the same dose, although the difference between the effects of these two forms of exposure to all intents and purposes is small.

A considerable qualitative difference in the reactions of the higher nervous functions is discovered in a comparison of early reactions to irradiation in both groups. However, chronic irradiation in the first days, when the administered dose was only 6-12 r, caused a deterioration of higher nervous activity, expressed in an increase of the number of phase phenomena (fig. 5). In the course of the first two days after beginning of irradiation in the chronically irradiated rats, adjustment phases were recorded in 16 of the 22 experiments; in 12 cases phase phenomena were observed at the intermediate and low levels. Among the acutely irradiated rats on the first two days after irradiation there was not a single experiment with phase phenomena at the low and intermediate levels. In the course of the third and fourth days after the onset of irradiations, when the administered doses were 18-24 r, in the group of chronically irradiated rats adjustment phases were observed at the in- 189 termediate and low levels in 18 of the 22 experiments. On the third and

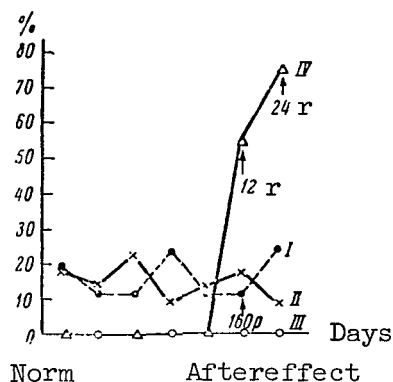


Figure 5. Effect of whole-body chronic and acute gamma irradiations of rats on number of phase phenomena in early stages after exposure. Along x-axis -- time in days (each point -- experiments for 2 days). For acute irradiation: I -- adjustment phases at high level; III -- adjustment phases at intermediate and low levels. For chronic irradiation: II -- adjustment phases at high level; IV -- adjustment phases at intermediate and low levels.

fourth days after acute irradiation adjustment phases were observed in only 4 of 16 experiments, and in all cases the phase phenomena were at a high level.

It therefore appears that the reaction of the higher parts of the brain on the first days after acute irradiation in a dose of 160 r develops more slowly and transpires far more easily than after chronic irradiations with the administration of far smaller doses. A well-expressed protective inhibition is observed only in the latter case.

Figure 6 shows the dynamics of changes of the number of impairments of higher nervous activity among the chronically irradiated rats during the entire period of irradiation. The illustration shows that after a sharp increase of impairments of higher nervous activity on the first days of irradiation, upon reaching an administered dose of 30 r the higher nervous activity of the rats improved somewhat. When the total dose increased from 50-72 r, it was higher than at the beginning of the irradiations, but did not reach the initial level. A new deterioration began when the total dose reached 96 r. At that time severe impairments of higher nervous activity began to appear. We see that the radiosensitivity of the higher parts of the CNS changed /190 substantially in the process of chronic irradiations. After an initial sharp reaction to irradiation there was a period of considerable decrease of the effectiveness of the irradiations.

However, this phenomenon of singular adaptation to irradiations exerted no influence on the final result. Upon administration of the total dose the

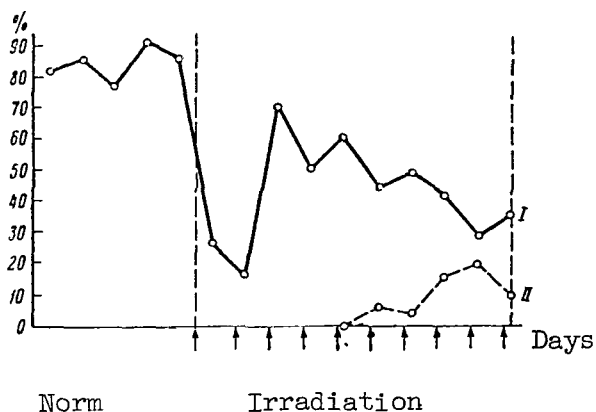


Figure 6. Effect of whole-body chronic gamma irradiations in daily dose of 6 r on higher nervous activity of rats. Along x-axis -- time in days (each point -- experiments for 2 days). I -- experiments with normal higher nervous activity; II -- experiments with severe impairments of higher nervous activity.

impairments of higher nervous activity after chronic irradiation were not less than after acute exposure in the same dose. The irradiations administered in the period of enhanced radioresistance participated in the final effect (at least outwardly) the same as those exposures which caused a maximum radiation reaction. /191

In contrast to the reaction of the higher parts of the brain, the changes of the hematological indices were far more severe in the group of rats subjected to acute irradiation. These data are shown in figure 7.

We did not statistically process the results of hematological investigations since the problem of the role of the time factor in the effect of irradiations on the blood system has been well studied.

Our only objective was to make sure that the results of our experiments in this field did not differ from the data in the literature.

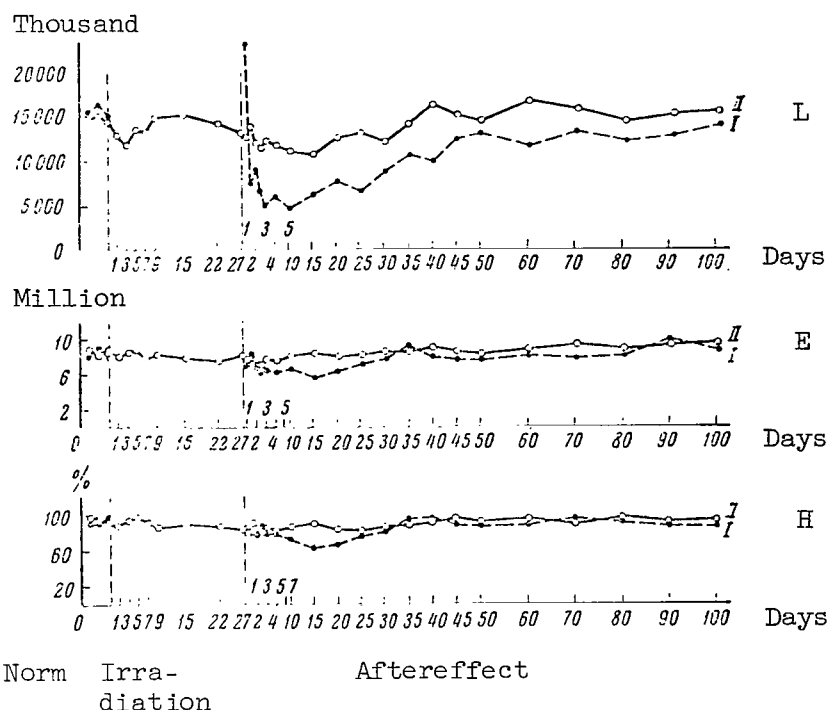


Figure 7. Effect of whole-body chronic and acute gamma irradiations on hematological indices of rats.
 Along x-axis -- time in days. Along y-axis --
 L -- leukocytes, thousand per 1 mm³ of blood;
 E -- erythrocytes, million per 1 mm³ of blood;
 H -- hemoglobin in percent (Sahli method);
 I -- acute irradiation; II -- chronic irradiation.

Conclusion

In a quantitative comparison of the effect of acute and chronic irradiations in equal doses on the conditioned reflexes it was demonstrated that the effect of chronic irradiations in no way is less than the effect of acute irradiation.

The decrease of the conditioned reflexes, determined from the change of their mean monthly values, in the groups of rats subjected to acute and chronic irradiations, revealed close agreement. The number of phase phenomena and other impairments of higher nervous activity in both groups was extremely close. Among the chronically irradiated animals the effect of the exposure was a little more clearly expressed than among the rats subjected to acute irradiation. This difference was small, but according to some indices was statistically reliable.

A considerable difference between the effect of chronic and acute irradiations is observed on the first days after exposure. After the acute irradiations in our experiments there was a latent period with a duration from three to six days (for most of the animals it was five days), during which there were no appreciable changes of conditioned reflex activity.

Among the rats subjected to chronic irradiation the latent period to all intents and purposes was absent and the impairments of higher nervous activity were completely clear even on the first days of irradiation when the administered dose was far lower than after acute exposure.

We may consider it established that for the doses which we used, chronic irradiations cause changes of higher nervous activity which are as pronounced as in acute irradiations. According to some indices, the impairments of higher nervous activity among the chronically irradiated rats were more clearly expressed than for acute irradiation.

At the same time that some of our experiments were made, our group also carried out investigations of the influence of acute and fractional irradiation on the unconditioned motor defense reflexes of a rabbit (M. A. Kuznetsova) and the influence of brief and prolonged irradiations on the electrical resistance of the brain tissue of rats (Z. I. Apanasenko).

Some of these investigations have been published by us jointly (Livshits, Meyzerov, Apanasenko, Kuznetsova, 1961, 1962).

M. A. Kuznetsova (1961) demonstrated that general fractional X-irradiation in a single dose of 10 r, administered five times per week until reaching a total dose of 400 r, and single acute irradiation in this same dose, exerted a similar effect on the latent period of the unconditioned defense flexor reflex of a rabbit's leg.

Z. I. Apanasenko (1961) found that total single gamma irradiations in 193 a dose of 600 r with a dose intensity of 0.5 r/min cause sharper changes of the electrical resistance of the cerebral tissues than irradiations with a dose intensity of 600 r/min. These data were obtained by the author on the basis of statistical data with good reliability ($P < 0.001$). On the basis of these studies it could be concluded that the absence of a direct dependence between the damaging effect of irradiation on the functions of the nervous system and dose intensity is standard for the different parts of the CNS. In many cases there is a higher degree of damage of the nervous system in the case of irradiations with a lesser dose intensity.

Our experiments show that the attenuation of effectiveness observed during chronic irradiations during a definite period in no way is reflected in the final result of the exposure. The effect of chronic irradiation is not weaker than the effect of acute irradiation in the same dose.

The "radiation memory" of the higher parts of the CNS completely sums the radiation effects, regardless of the degree of the functional changes caused by them.

G. S. Strelin (1956, 1962) feels that the radiation effects are in direct dependence on dose intensity in tissues having high proliferative activity, because repair processes transpire intensively in them. On the other hand, tissues with weak proliferative activity do not have the capacity for repair of radiation damage, and the effect of irradiations on them does not depend on dose intensity. This situation clearly explains the absence of a direct dependence of the effect of radiations on the functions of the CNS on dose intensity and the capacity of the nervous system for complete summing of the effect of chronic and fractional irradiations. However, this cannot serve as an explanation for the more significant damage of the nervous system during prolonged irradiations than during brief irradiations. This problem requires additional investigation, both experimental and theoretical.

Our data differ from the results of investigations by Hicks et al., 1958, McLaurin et al., 1955, and Berg and Lindgren, 1958. These authors discovered a considerably sharper damaging effect on the structure and functions of the CNS during acute and brief irradiations than during fractional and prolonged irradiations.

This difference can be attributed to the fact that we and those investigators used different ranges of doses. In our experiments and the experiments of M. A. Kuznetsova and Z. I. Apanasenko sublethal or minimum lethal doses were used (160, 400 and 600 r, respectively). The authors discovered a direct dependence between the effect of irradiation on the CNS on dose intensity, 194 and then irradiated animals in doses of several thousand r. It is entirely probable that the key mechanisms of the reaction in these ranges of doses are different. In particular, it is extremely possible that with exposure in high doses the key role is played by the effect of radiations on the vascular system, which is directly proportional to dose intensity (Berg, Lindgren, 1958; Corp, Neal, 1959, and others).

At the same time, we admit that other factors may play a role. The literature contains data indicating that the parts of the CNS in a state of high functional activity are damaged more severely by ionizing radiation than parts of the CNS in a state of rest (Sokolova, 1962).

In an alert animal in a state of relative rest, a definite number of neurons are in a state of high functional activity. Therefore, in the case of chronic irradiations there are a greater number of functionally active neurons affected by radiation than in the case of brief irradiation. Under the influence of small doses of radiation there is greater damage to functionally active neurons. With exposure to greater radiation doses, such as used by McLaurin, Hicks, Berg and Lindgren, the functional state of the neurons exerts a smaller influence on the effect of irradiation, because doses of several thousand r also damage neurons in a state of low radioresistance. This hypothesis was proposed by N. N. Livshits at a conference on the problems of the effect of small doses of ionizing radiation on physiological functions in 1961.

It is possible that with still higher doses (some tens of thousands r) and very high dose intensities (hundreds and thousands r/min) the key role will be played by other mechanisms and the dependence of the reaction on dose intensity

will become the opposite (Domshlak et al., 1959; Koznova and Khrushchev, 1960; Darenskaya et al., 1961).

In such exposures the effect of irradiations on hematopoiesis is also inversely proportional to dose intensity (Kalyayeva, 1960).

In a discussion of the results of experiments on the influence of chronic irradiations of the head on the higher nervous activity of dogs (Livshits, Meyzerov, 1963), still another hypothesis was expressed on the mechanism of these phenomena.

We assumed that the cause of the relatively weak effect on the functions of the higher parts of the brain by acute irradiations is the more clearly expressed activation of compensatory mechanisms during acute irradiations than is the case in chronic irradiations. We consider the participation of this /195 mechanism together with those mentioned above to be highly probable.

Such explanations are preliminary, and this problem requires additional study.

The results of our experiments, in full agreement with the data obtained by Z. I. Apanasenko and M. A. Kuznetsova, show that in the case of chronic irradiations in doses which we used, the specific weight of the functional disruptions of the CNS in the general radiation reactions of the body is greater than in the case of acute irradiations, which must be taken into account in occupational pathology and hygiene.

Our conclusions, drawn on the basis of experiments on animals, coincide with data from medical neurological examinations of persons subjected to occupational chronic irradiation in small doses (Danilin et al., 1960; Lysina, 1958; Kyandaryan et al., 1960; Abuladze, 1961; Gus'kova, 1962, and others).

I regard it as my pleasant duty to express sincere appreciation to Doctor of Biological Sciences N. N. Livshits for the proposed theme and guidance of the work.

Summary

1. During chronic irradiation, reactions of higher parts of the CNS changed appreciably. After sharp impairments of the higher nervous activity observed on the first days of irradiation, there was a phase of some improvement of higher nervous activity, despite the fact that the irradiation was continued. However, this temporary increase of resistance exerted no influence on the final result of irradiation.

2. Whole-body chronic gamma irradiation (6 r/day; total dose 160 r) and whole-body acute irradiation (160 r; 85 r/min) exerted a similar effect on the conditioned reflex activity of rats. According to some indices, impairments

of higher nervous activity were more severe in rats subjected to chronic irradiation. Here, the difference was small, but statistically reliable.

3. The decrease of the content of leukocytes, erythrocytes and hemoglobin in the peripheral blood was expressed far more sharply in rats subjected to acute irradiation than in chronically irradiated animals.

4. In the case of chronic irradiations in the doses which we used, the specific weight of the impairments of functions of the CNS in the radiation reactions of the body was higher than in the case of acute irradiations.

5. A hypothesis is presented on the reasons for the discrepancy between the results in our experiments and the data of foreign authors, obtained /196 during irradiations in doses of thousands of r, showing a direct dependence between impairments of the structures and functions of the CNS on dose intensity. It is postulated that the key role in the development of radiation damage is played by different mechanisms in different ranges of doses. In particular, in the reactions of the CNS to irradiations in high doses a considerable role may be played by the vascular factor. At the same time, it is postulated that in the case of chronic irradiations a greater number of functionally active neurons are subjected to a radiation effect than in the case of brief single irradiation.

EFFECT OF CHRONIC GAMMA IRRADIATION ON FUNCTIONS OF THE
VESTIBULAR ANALYZER AND THE ROLE OF THE TIME FACTOR
IN RADIATION REACTIONS OF THE NERVOUS SYSTEM

Z. I. Apanasenko

ABSTRACT

Male guinea pigs were exposed to prolonged gamma irradiation with 500 r and a dose intensity of 0.6 r/min. The bioelectric activity of extensors of the rear extremity (hind leg) were investigated before, during and after adequate stimulation of the vestibular analyzer. Survival rate, weight and general clinical state of the animals also were studied.

Prolonged irradiation induces strong and long-term changes of the electromyographic characteristics of the vestibular-tonic reflex for the muscles of the rear extremity. These changes are greater and qualitatively different from those induced by acute irradiation in the same dose. All animals survived; the severity of radiation sickness and the changes in the peripheral blood are less than after acute irradiation.

Information on the influence of penetrating radiation on the vestibular apparatus began to appear in the scientific literature more than 50 years ago. Cases of the appearance of vestibular disorders after chronic radiation exposures have been noted by many clinicians (Voyachek, 1910; Kurshakov, 1954; Blagoveshchenskaya, 1956; Titov, 1957; Moskovskaya, 1958, 1959; Donato, 1926). In most cases symptom complexes were observed of more or less clearly expressed labyrinthitis: impairments of gait, dizziness, spontaneous nystagmus, optical-vestibular impairments, etc. /197

In experimental investigations it was also found that there were functional and morphological impairments in the structures of the vestibular analyzer after exposure to penetrating radiation. Among the functional impairments were nystagmus of position and atypical deflection of the eyes (Mil'shteyn, 1939; Zlotnikov, 1958); rotational movements in the direction of the injured labyrinth (Thielemann, 1929; Quastler, 1957) and appearance of spontaneous nystagmus and impairment of coordination of movements and orientation in space (Minayev, 1962; Quastler, 1957, Clemente et al., 1958). There was a change of the unconditioned and conditioned vestibular reflexes (Petelina, 1957, 1958),

appearance of vestibular ataxia (Minayev, 1962) and symptoms of labyrinthectomy (Ewald, 1905).

The morphological changes are also quite varied. As a result of irradiation there were frequent hemorrhages, minute cellular infiltration, defects of the nerve fibers and degenerative changes in the vestibular Schwalbe, Deiters and Bechterew nuclei (Marx, 1909; Thielemann, 1929; Khilov, 1927; Zlotnikov, (1958).

T. N. Mil'shteyn (1939) observed the appearance of an exudate under the membranous base of the utricle; I. A. Lopatko (1939) discovered necrosis of the soft tissues of the labyrinth with subsequent atrophic changes and even with detachment of the otoliths of the utricle.

Nevertheless, the problem of the influence of penetrating radiation /198 on the functions of the vestibular apparatus still remains inadequately studied.

Few specialized experimental investigations have been conducted on animals. Available clinical and experimental data in large part are random and contradictory. For example, N. V. Moskovskaya (1958, 1959), under clinical conditions, in X-ray therapy for malignant tumors (5,000-12,000 r in the region of the neck or chest), discovered an increase of excitability of the vestibular analyzer at the time of and after irradiation. The author also cites the similar results of Donato (1926), obtained after local irradiation by X-rays.

Exactly opposite results were obtained by other authors. A. I. Titov (1957) analyzes the results of observations of individuals subjected to prolonged exposure to penetrating radiation in small doses during work with sources of ionizing radiation. The author notes a substantial change of the normal relation of sensory, somatic and autonomous reactions. The results were ambiguous, but in most cases there was an inhibition of vestibular-somatic reactions. A decrease of the values of positive conditioned reflexes to rotation and the appearance of phase phenomena were observed by V. V. Petelina (1957) after total irradiation of dogs with 400 r.

A decrease of the excitability of the vestibular analyzer was discovered by Yu. G. Grigor'yev (1962) under the influence of irradiation of the body in large doses.

A. A. Sveshnikov and A. V. Sevan'kayev (1962, 1963, 1964) investigated the threshold sensitivity of the semicircular canals to angular acceleration, the reactance of the vestibular analyzer and the character of vestibular-somatic (postrotational nystagmus) and vestibular-autonomous (respiration, pulse,

blood pressure) reflexes after irradiation of rabbits by Co^{60} gamma rays in different doses. After administration of a dose of 100 r the changes were unstable and varied, but in most cases the reactance of the vestibular analyzer was somewhat increased. After irradiation in a dose of 200 r there was a regular decrease of excitability and the reactivity of the vestibular analyzer. Doses of 500-5000 r led to strong depression of the functions of the labyrinth.

In addition to the ambiguity, the materials of different authors are difficult to compare, because very frequently (especially in clinical work) random observations are cited, based on spontaneous vestibular symptoms; an adequate dosed stimulus (except in the studies of Yu. G. Grigor'yev and his associates) is rarely used. In addition, it is known that radiation reactions of the vestibular analyzer, like any other system of the body, depend on the conditions of irradiation: the type of radiant energy, dose, places of its application, dose intensity, fractional administration of irradiation, intervals /199 between irradiation, etc. The data accumulated in the field of radiobiology of the organ of equilibrium usually have not been analyzed from this point of view. In many studies the irradiation conditions are not even indicated. Although the dependence of radiation reactions of the labyrinth on irradiation dose is mentioned in some studies, data on the influence of irradiation dose intensity on the investigated functions could not be found in the literature. The only pertinent treatment is the morphological study of I. A. Lopatko (1939), which is an investigation of the changes in the inner ear in relation to dose and irradiation method. The author notes that fractional irradiation is sometimes more effective.

In our earlier investigations (Apanasenko, Kuznetsova, 1964; Apanasenko, 1964) it was demonstrated that acute gamma irradiation of guinea pigs in a dose of 500 r with a dose intensity of 261 r/min leads to a depression of the functions of the vestibular analyzer. A change of the electromyographic characteristics of the vestibular-tonic reflexes for the muscles of the rear extremities indicated a decrease of the reaction of the otolithic apparatus.

Our study included an investigation of the characteristics of the radiation reactions of the vestibular analyzer during prolonged administration of the same dose of Co⁶⁰ gamma rays. Clarification of the dependence of the radiation reactions of the labyrinth on dose intensity in our case was found to be all the more feasible, because the possibility of quantitative comparison was ensured by rigorously identical experimental conditions.

As in the case of acute irradiation, the work was done with male guinea pigs weighing 350-500 g.

Observation of the animals began 10-15 days before irradiation.

After establishing stable values for the investigated parameters, the guinea pigs were subjected to Co⁶⁰ irradiation in a dose of 500 r with a dose intensity of 0.6 r/min. Continuous, almost 14 hr irradiation, was always done in the evening and night hours. The control animals during this period were maintained under the same conditions, but were not subjected to irradiation. The examination of the animals began 2-2.5 hr after the end of irradiation and then after 1, 2, 3, 5, 7, 10, 15, 20, 25 and 30 days. The control animals were always investigated in the same way and at the same times. The experimental group included 12 animals and the control group included 14.

The functional state of the vestibular analyzer was evaluated on the basis of the electromyographic characteristics of the vestibular-tonic reflexes for

the muscles of the rear extremities. The electromyograms were recorded with plate silver electrodes from a group of extensors. The recording was done on movie film, using a loop oscillograph. The electromyograms were simultaneously integrated with a specially designed integrator and were expressed in /200 relative units on the indicators of a mechanical counter.

The recording of the electrical activity of the muscles was done for three successive 10-sec periods: at rest (the animal seated in the chamber in a normal pose), during adequate stimulation of the vestibular analyzer and directly after such stimulation. The time marks and the records of the stimuli on the films were used to compute the values of the latent period and the duration of the aftereffect of the reaction to the vestibular test.

As an adequate vestibular stimulus we used measured rotational oscillation of the animal about the longitudinal axis of the body on a special apparatus for a period of 10 sec, with a frequency of 0.6 cps and an angle of inclination of 25°.

Thus, the specific character of the stimulus and the selected tests determined the investigation of the functions primarily of the otolithic part of the labyrinth. According to the classical investigations of Magnus (1924), the initial cause in the tonic contraction of the muscles of the extremities is stimulation of the otolithic apparatus, and specifically, the apparatus of the utricle.

In addition to the electromyographic investigation of the state of the organ of equilibrium, there was regular observation of the peripheral blood, weight, temperature, general clinical state and survival rate of the animals.

All results were processed statistically using the median and dispersion (F) tests.

As in the earlier investigations, the myograms recorded prior to irradiation were rather uniform and had a normal appearance: uniform fluctuations of potential with an amplitude of 10-50 μ V at rest, high-amplitude groups of pulses (150-400 μ V) during stimulation of the vestibular analyzer and a residual increased impulsation in the aftereffect. The mean duration of the aftereffect was 2-4 sec; the value of the latent period of the electromyographic reaction to vestibular stimulation was approximately 0.01-0.3 sec. Accordingly, the mean integral values of electrical activity prior to irradiation persisted from experiment to experiment at a definite stable level for each of the three investigated periods: rest, reaction and aftereffect. The observed insignificant fluctuations about the mean value did not exceed the limits of the physiological norm.

Prolonged irradiation with 500 r causes a strong and prolonged change of the bioelectric activity of the investigated muscles, both at rest and at the time of the response reaction to vestibular stimulation, and does not decrease the radiobiological effect on the investigated vestibular-tonic reflex.

In most cases the radiation reactions during prolonged irradiation were even more considerable than those for acute irradiation. Very frequently /201

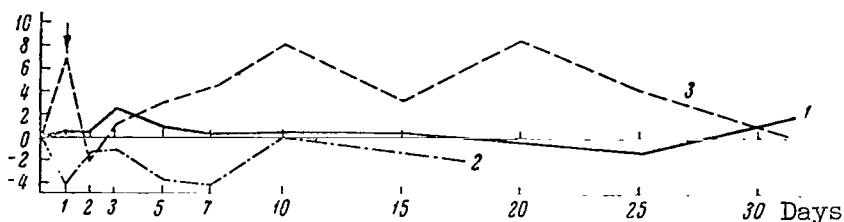


Figure 1. Change of background electrical activity of muscles after prolonged and acute irradiations. Along x-axis -- time after irradiation, in days. Along y-axis -- integral bioelectric activity of muscles in relative units. 0 value represents mean relative value of electrical activity prior to irradiation. 1, Control; 2, acute irradiation; 3, prolonged irradiation. Arrow denotes day of irradiation.

the effects of brief and prolonged irradiation differed from one another both quantitatively and qualitatively.

The results are analyzed on the basis of the values of the integral myoelectric activity. For comparative purposes, we show the earlier recorded results of acute irradiation with the same dose in all figures. The lesser period of observation for acute irradiation can be attributed to the fact that the experiments were interrupted by the death of the animals. On the graphs we have used mean data for all animals of each group.

In the initial processing of the results for each group we computed the deviation from the mean value of electrical activity prior to exposure. Then all data before and after exposure were divided by this mean group deviation, after which the mean norm prior to the exposure was assigned a zero value, and the values for the days after the exposure were plotted off along the y-axis in relative units. This initial analysis method detects only those changes which obviously exceed the level of the mean value and the mean deviations from this value prior to irradiation.

Figure 1 shows the dynamics of the background activity of the group of extensors of the rear extremity of guinea pigs after irradiation. The graph clearly shows that the changes caused by prolonged irradiation considerably exceed in value the changes which appeared after acute irradiation with the same dose. In addition, there is a completely different direction of the changes: after acute irradiation the muscular electrical activity at a state of relative rest decreases immediately and stably, and after prolonged irradiation there is an increase of the background electrical activity of the investigated muscles. During the entire month-long period of postradiation observation, there was some decrease of the curve below the initial level only on the second day. This drop reflects the decrease of myoelectric activity, which occurs in half 202 (seven guinea pigs) of the animals on the second-third day after irradiation.

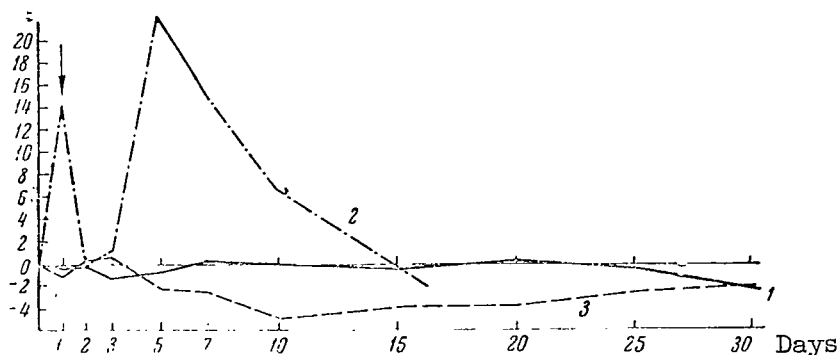


Figure 2. Change after prolonged and acute irradiation of electrical activity of muscles during stimulation of vestibular analyzer. Notations same as in fig. 1.

On the remaining days the myoelectric activity at rest is maintained at a high level. Naturally, there are fluctuations of the values of background electrical activity in the course of the experimental period, characteristic of any physiological process. In most of the experimental animals the background electrical activity decreases somewhat (remaining considerably above the control on the 15th day after irradiation, but on the 20th day it increases again. Approach to the control level begins on the 25th day after exposure.

The observed changes are of the same sign for the 11 irradiated animals (except for the changes on the second day). Only in one guinea pig, the background electrical activity remained somewhat lower than the initial data from the second day after irradiation. The changes were statistically reliable according to both the median and dispersion tests. The median increases by 3.2 units in comparison with the control and by 1.6 units in comparison with the level of the experimental group prior to irradiation ($P < 0.01$). The dispersion (fig. 9) increases greatly, both in comparison with the initial level prior to irradiation and in comparison with the control ($P < 0.001$). Comparison with the results of acute irradiation also establishes completely reliable statistical differences (for the median $P < 0.01$; for the dispersion $P < 0.001$). The median in the case of prolonged irradiation increases by 4.46 units, and dispersion increases by a factor of 3.75.

Figure 2 shows the postirradiation change of muscular electrical activity at the time of adequate stimulation of the vestibular analyzer. On the first three days after prolonged irradiation the changes do not exceed the limits of fluctuations of the control. On these days the effect varies in sign in different animals. Beginning with the fifth day, the electromyographic reaction to vestibular stimulation falls below the norm and remains at this relatively low level for a long time. As in the case of the background electrical activity, the changes in their character in this case also differ from those after acute irradiation. The nonuniformity of the results and the

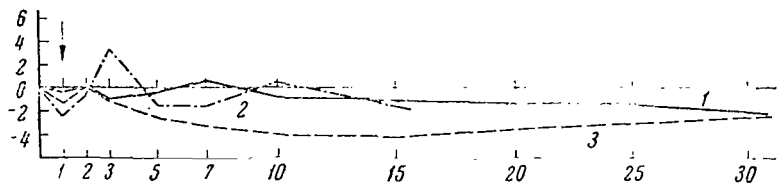


Figure 3. Postirradiation change of electrical activity of muscles in aftereffect to stimulation of vestibular analyzer. Notations same as in fig. 1.

pathological increase of the reaction to stimulation of the organ of equilibrium, characteristic of the effect of acute irradiation, are absent here. The radiation effects are identical for all animals of the experimental group. The dispersion for this reason decreases sharply (fig. 9); the median decreases by two units in comparison with the effect of acute irradiation. The influences of prolonged and acute irradiations statistically differ reliably from one another ($P < 0.001$). The differences from the initial level and from the control are also statistically reliable ($P < 0.001$ both with respect to the medial test and the dispersion test). The median decreases by 2.5 units, and the dispersion approximately doubles.

Figure 3 illustrates the effect of prolonged irradiation on the aftereffect of the vestibular-tonic reaction. The electrical activity of the investigated extensors of the extremity in the aftereffect of the reaction to vestibular stimulation decreases after prolonged irradiation. The effect is very prolonged. Up to the 30th day after irradiation the curve for the experimental group is situated considerably below the control curve. Convergence of the curves of the experimental and control groups occurs only on the second and third days after irradiation. These values, differing little from the control, appeared due to the presence of high myoelectric activity in the individual irradiated animals on these days, which led to a smoothing of the results during averaging. After the third day the changes become uniform for all experimental animals. The differences between the control and the initial level were statistically reliable ($P < 0.001$). The median decreases by three units in comparison with the control and by 3.6 units in comparison with the initial level for the experimental group of animals. After irradiation ^{/204} the dispersion increases by a factor greater than 2. Comparison of the results of the acute and prolonged irradiations reveals that the latter exceeds the first in its effectiveness. The qualitative difference is in the greater stability and duration of the changes during prolonged irradiation. The wave-like shape of the curve characteristic of acute irradiation is absent in the case of prolonged irradiation. The dispersion of the values of muscular electrical activity decreases. The median after prolonged irradiation lies 1.8 units lower than after acute irradiation. According to both statistical criteria the differences between the results of the two types of irradiation are reliable ($P < 0.001$).

The change of the latent period of the reaction to adequate stimulation of the vestibular analyzer after prolonged irradiation is shown in figure 4.

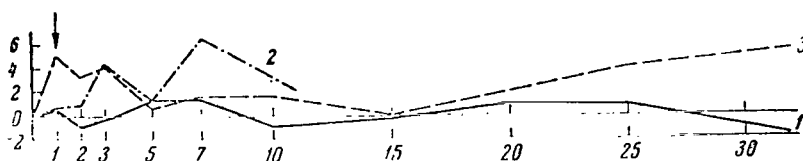


Figure 4. Change of value of latent period of electromyographic reaction to stimulation of vestibular analyzer after prolonged and acute irradiations. Along y-axis -- value of latent period in relative units. 0 is the mean relative value of latent period prior to irradiation. Remaining notations same as in fig. 1.

The latent period of this reaction is the same as after acute exposure, that is, it increases. This increase has a biphasic character; it was expressed sharply on the first three days after irradiation; in the period from the 5th to the 15th day the values are somewhat normalized, but after the 20th day there is again an increase of the latent period. In individual animals in these phases of increase the delay of the response reaction to vestibular stimulation attains considerable values, so that the reaction to all intents and purposes begins only with the second testing oscillation. Among the entire group of experimental animals there was only one in which the value of the latent period of the investigated reaction almost did not change after prolonged irradiation, and in one guinea pig it decreased. The differences from the control were statistically reliable according to the dispersion test (the dispersion increases by a factor of 14, $P < 0.001$); the median changes without sufficient reliability ($P > 0.05$). Comparison with the corresponding effect of acute irradiation reveals an interesting detail: the curve representing the effect of acute irradiation also has two peaks. However, here both peaks are close together and the periods are of short duration, but in the case of prolonged irradiation the "waves" seemingly are drawn out, and the periods of increase and decrease of the values transpire slowly. The dispersion is 2.3 times less than in the case of acute irradiation. In the first period after exposure (first 10 days), the effectiveness of prolonged irradiation according to this index is a little lower than the effectiveness of acute irradiation. The difference is small, however, and does not exceed the limits of triple the error. For this reason the differences between the compared groups are statistically reliable, according to the dispersion test ($P < 0.001$), and unreliable according to the median test ($P < 0.05$).

The aftereffect of the investigated reaction after prolonged irradiation (fig. 5) is greatly shortened, especially from the fifth day after irradiation. As already observed more than once on the basis of other indices, on the first three days (especially on the second day) there is some difference in the variability of effects among different animals. Then the changes become the same and stable. A return to the norm begins after the 15th day, but only partially. Total normalcy was not observed even a month after irradiation. The differences from the control were statistically reliable according to the medial test

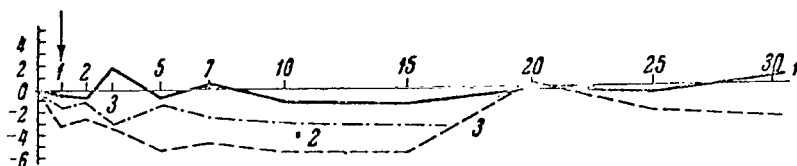


Figure 5. Postirradiation change of aftereffect of electromyographic reaction to stimulation of vestibular analyzer.

Notations same as in fig. 1.

($P < 0.001$), and the dispersion of the values of the duration of the aftereffect after prolonged exposure remains within the limits of fluctuations of the control ($P > 0.05$). The effect of prolonged radiation in this case is more significant, compared with the effect of acute irradiation. With prolonged irradiation the aftereffect of the vestibular-tonic reaction is shortened to a greater extent. The curve representing prolonged exposure during the entire period of observations lies below the curve representing the effect of brief exposure. There is no basic qualitative difference between the effects of the compared methods of irradiation, according to this index. Reliability of the differences between the groups of acute and prolonged irradiations is noted for both statistical criteria ($P < 0.001$ for dispersion and $P < 0.05$ for the median). With prolonged irradiation the dispersion of the values of the duration of the aftereffect decreases by a factor of 2.3 as compared with acute exposure. /206

Thus, almost all electromyographic characteristics of the investigated vestibular-tonic reflex change more considerably after prolonged irradiation. Completely different relations are observed in comparison of survival rates of the animals and the reactions of the peripheral blood. According to these indices, acute irradiation is more effective, agreeing fully with the data in the literature. Only 1 of the 10 animals survived after acute irradiation. Death occurred on the 9th-14th day, with manifestations of acute leukopenia, radiation pneumonia and hemorrhages in the subcutaneous tissue and internal organs. In the case of prolonged irradiation all 12 of the experimental animals survived; external clinical symptoms of acute radiation sickness were not observed (fig. 6). Figure 7 shows the change of the number of leukocytes in the peripheral blood after irradiation. Under the influence of acute irradiation there is a sharp and statistically reliable ($P < 0.001$) decrease of the number of leukocytes, characteristic of acute radiation sickness, beginning on the second-third day after exposure. On the day of irradiation leukocytosis was observed in many of the animals, which according to references in the literature is a forerunner of a more severe course of the sickness and an earlier death. In the premortality period the number of leukocytes decreased sometimes to 500 and even to 300-250 per 1 mm³ of blood. The minimum absolute mean number of leukocytes for the entire group was observed in the case of acute

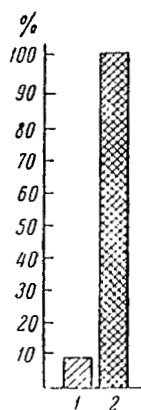


Figure 6. Diagram of survival rate of animals after acute and prolonged irradiations.

Along y-axis -- percentage of surviving animals on 30th day after irradiation.
1, Group subjected to acute irradiation;
2, group subjected to prolonged irradiation.

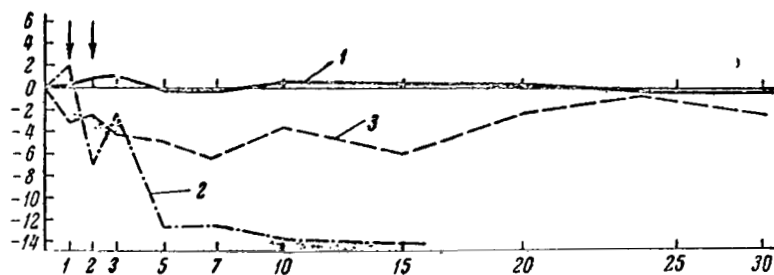


Figure 7. Change of the number of leukocytes in peripheral blood of animals after prolonged and acute irradiations.

Along y-axis -- number of leukocytes per 1 mm^3 of blood, expressed in percent of mean norm (0 on graph) and related to mean deviation for each group from norm prior to irradiation. Remaining notations same as in fig. 1.

irradiation on the 10th day and was 810 per 1 mm^3 . Prolonged irradiation also causes a statistically reliable ($P < 0.001$) decrease of the number of leukocytes in the peripheral blood. However, this decrease never was so sharp and significant as after acute irradiation. Leukopenia of intermediate severity develops gradually. The minimum mean quantity of leukocytes for the group is 3650 per

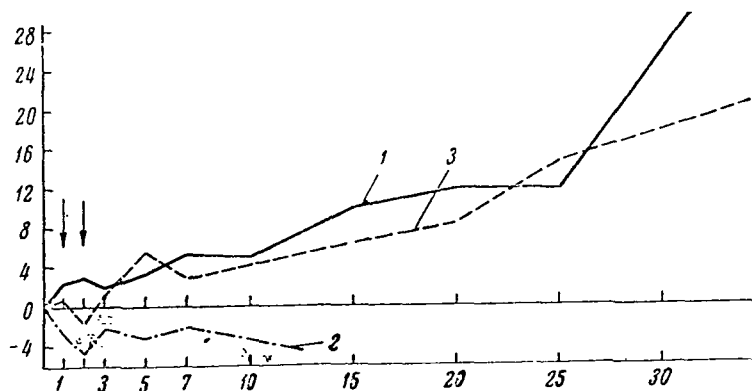


Figure 8. Change of weight of animals after prolonged and acute irradiations.

Along y-axis -- weight, expressed in percent of mean norm (0 on graph) and related to mean deviation for each group from norm prior to irradiation. Remaining notations same as in fig. 1.

1 mm³ of blood. During the entire period of the observations the level of leukocytes did not fall below 2100-2250 per 1 mm³ of blood in a single animal of this group. The leukocytosis on the first day after the exposure was also not typical for acute irradiation. Gradual normalization of the number of /207 leukocytes begins after the 15th day. The difference between the effect of acute and prolonged irradiations on the cell composition of the peripheral blood is statistically reliable ($P < 0.001$)

The weight of animals irradiated in large and small dose intensities changes completely differently (fig. 8). Among the control guinea pigs there is a normal gradual increase of weight with time. The weight of acutely irradiated animals began to decrease from the first day after irradiation and /208 was maintained at such a low level right up to the time of death. The difference from the control was reliable ($P < 0.001$). The guinea pigs subjected to prolonged irradiation begin a quite rapid gain of weight beginning on the third day. Weight increase is observed thereafter during the entire experimental period.

The dynamics of the weight of the animals after prolonged irradiation statistically differ reliably from the dynamics after acute irradiation ($P < 0.001$), and to all intents and purposes do not differ from the control.

Conclusions

These investigations revealed a clearly expressed dependence of the radiobiological effects on the irradiation dose intensity. The influence of the

so-called "time factor" on the radiation reactions of the organism was established long ago in radiobiology. Most of the studies made on this problem have used survival rate as the index. Numerous investigations demonstrate the direct dependence of the mortality of the animals on the value of dose intensity (Koznova, Glazunov, Vitushkin, 1962; Moskaliev, 1961; Strelin et al., 1957; Brown et al., 1960; Corp and Neal, 1959; Howard et al., 1955; Logie et al., 1960; Neal, 1960; Paterson, 1944; Paterson and Thomson, 1948; Sinov and Lofstrem, 1962; Stearner and Tyler, 1957; Thomson and Tourtellotte, 1953, and others). However, when using large doses, small intensities of fractional irradiations sometimes prove to be more harmful (Darenskaya et al., 1961; Kalyayeva, 1958; Moskaliev, 1960; Cole et al., 1960; Mole, 1959).

In our study very large radiation doses were not used. The mortality of the animals and the severity of the radiation sickness in the case of prolonged irradiation decreased considerably (time factor > 1), which fully agrees with the basic data in the literature.

With respect to the characteristics of the vestibular-tonic reflex, no direct indications on the problem with which we were concerned could be found in the literature. In the past decade studies have appeared which are devoted to investigation of the effect of different radiation dose intensities on a number of physiological and morphological indices (Kozlova, 1960; Grayevskaya, Keylina, 1955; Fastyuchenko, Varshavskiy, 1957; Ronichesvskaya, 1959; Strelin, Galkovskaya, 1961; Strelin, 1962; Moskaliev, 1960; Quastler et al., 1959; Baum and Kimelsdorf, 1957; Cole et al., 1958).

Despite such a variety of studies, little attention has been given to the influence of the "time factor" on the radiation reactions of the nervous system. The individual available facts are contradictory and were obtained under different experimental conditions. McLaurin et al. (1955) used monkeys in an investigation of the occurrence and severity of paralysis, the rate 209 of passage of nerve pulses through the spinal cord and bioelectric currents

of the spinal cord during its local irradiation by Ta^{182} . It was found that there is a direct dependence of the investigated reactions on the rate of administration of the dose; the magnitude of the dose was of secondary importance. The direct influence of the "time factor" on the morphological and physiological changes in the CNS after total irradiation of mice and rats was also detected by Hicks, Wright and Seigh (1956). However, in these studies very large radiation dose intensities (thousands and even tens of thousands r) were used, and therefore it is impossible to compare our results with these investigations.

The dependence between dose intensity (from 0.013 to 7.5 r/sec) and the duration of the irradiation, at which a depression of the bioelectric activity of the cerebral cortex can be observed in rabbits, was investigated by A. B. Tsy-pin and Ya. G. Grigor'yev (1960). The changes appeared earlier and were more sharply expressed for large dose intensities (to a certain limit).

With respect to the magnitude of the doses used and the direction of the influence of the time factor, our work is similar to the laboratory investigations of N. N. Livshits. During fractional and chronic irradiations of dogs

in sublethal and minimum lethal doses (300-450 r) it was found that there is a discrepancy between the deterioration of conditioned reflex activity and the severity of radiation sickness. In fractional and chronic irradiations the cortical activity of animals was injured to an equal degree or even somewhat more strongly than during acute irradiations. The impairment of higher nervous activity at the time of slow irradiations was clearly expressed, although the clinical manifestations of radiation sickness could be absent (Livshits, 1956, 1961). Ye. S. Meyzerov (1959, 1962), using dogs and rats, demonstrated the high sensitivity of the cerebral cortex to fractional and chronic irradiations. With respect to effectiveness, such irradiations were equivalent to acute irradiation and frequently even exceeded it.

Similar results were also obtained by M. A. Kuznetsova (1961) in an investigation of the latent period of the unconditioned defense flexor reflex in rabbits. The possibility of the occurrence of severer impairments in higher nervous activity during fractional irradiation was also mentioned in a review by A. V. Lebedinskiy and Z. G. Nakhil'nitskaya (1960).

Our earlier study (Apanasenko, 1961) was devoted to the change of the radiation reactions of the CNS during prolonged irradiation. It was demonstrated that prolonged irradiation (600 r totally) changes the dynamics of the electrical conductivity of the cerebral cortex of rats to a greater degree /210 than acute irradiation. The mortality and the severity of the radiation sickness in this case decrease sharply.

The group of studies mentioned above was carried out under different radiation conditions (fractional, prolonged, chronic irradiation). This circumstance makes it possible to assert with great assurance that in the case of sublethal and minimum lethal irradiation doses for the radiation reactions of the CNS there is instead a characteristic inverse dependence on irradiation dose intensity. There is no attenuation of the damaging effect of radiation on the nervous system with an increase of exposure. Our results fully agree with this situation: the investigated characteristics of the vestibular- tonic reflex in almost all cases change more in the case of irradiation with a low dose intensity (table 1).

The observations of R. G. Golodets (1964) are indirect confirmation of the great sensitivity of the vestibular analyzer to the effect of low-intensity radiation. The author notes that the clinical examinations of physicians and X-ray technicians frequently reveal the presence of vestibular and optical-vestibular impairments (dizziness, nystagmoid twitching, decrease of /211 muscular tone, disarrangements of the static and locomotor coordination). This is the most characteristic phenomenon in the sphere of impairments of the animal nervous system in the case of chronic irradiation (the dose was 5-10 times greater than the admissible value).

We already have mentioned cases of the occurrence of labyrinthitis accompanying radiotherapy.

An investigation by Berge and Lindgren (1958) completely disagrees with these clinical observations and the results of our work. The authors discovered acceleration of the appearance of neurological symptoms (the most frequent of

TABLE 1. SOME RESULTS OF COMPARING THE EFFECTS OF ACUTE AND PROLONGED IRRADIATIONS.

Index	Quantitatively		Qualitatively	
	Acute	Prolonged	Acute	Prolonged
Bioelectric activity of muscles at rest	Less than	More than	Decrease	Increase
Bioelectric activity of muscles at time of adequate stimulation of vestibular analyzer	More than	Less than	Increase Changes variable, large scatter	Decrease Changes of same type, small scatter
Bioelectric activity of muscles in aftereffect of reaction to adequate stimulation of vestibular analyzer	Less than	More than	Wavelike fluctuations about zero level	Decrease
Latent period of myoelectric reaction to adequate stimulation of vestibular analyzer	Nearly identical	Nearly identical	Increase Rapid changes	Increase Slow changes
Duration of aftereffect of myoelectric reaction to adequate stimulation of vestibular analyzer	Less than	More than	Decrease	Decrease

these is vestibular-cerebellar impairments) with an increase of the rate of administration of the dose. In the case of definite small rates (administration of dose in 12 or 30 days), there were no vestibular-cerebellar impairments at all. The contradiction apparently can be attributed to the fact that in this case as well very large doses of local fractional irradiation (2100-9500 r on the head) were used. Our observation of a qualitatively different effect of acute and prolonged irradiation on the parameters of the vestibular-tonic reflex merits attention. According to nearly all investigated indices, the reaction to prolonged irradiation not only was greater in magnitude, but also had a qualitatively different character (table 1). The qualitative difference was expressed both in the direction of the effects and in the specific characteristics of their dynamics. In the case of irradiation with a low intensity, beginning on the third-fifth days after exposure there are characteristic prolonged stable changes with small fluctuations and a smaller scatter of

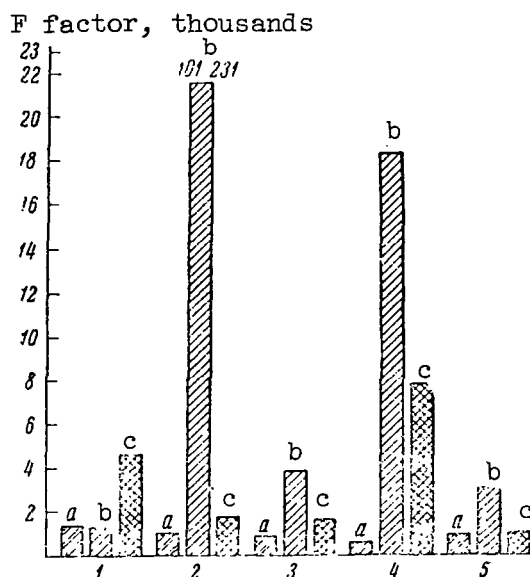


Figure 9. Diagram of values of F factor of dispersion of values of investigated parameters after acute and prolonged irradiations.

Along y-axis -- value of F factor in thousands.

1, Electrical activity of muscles in state of relative rest; 2, electrical activity of muscles at time of reaction to adequate stimulation of the vestibular analyzer; 3, electrical activity of muscles in aftereffect of reaction to adequate stimulation of vestibular analyzer; 4, latent period of this reaction; 5, duration of aftereffect of this reaction; a, control; b, acute irradiation; c, prolonged irradiation.

data than in the case of acute irradiation. For this reason the dispersion of the readings for the investigated parameters in the case of prolonged irradiation usually is considerably less than the dispersion for acute irradiation. Figure 9 illustrates the decrease of the F dispersion factor for prolonged irradiation for all investigated indices, except the background myoelectric activity. The functional state of the vestibular analyzer by no means is the only determining factor for the muscular electrical activity in a state of relative rest. As a result, somewhat different patterns of behavior may occur here.

On the first two-three days after irradiation there is some instability of the changes, and sometimes their sign is different for individual animals. This phenomenon can be attributed to the individual characteristics of the body and the different rate of the initial reactions after administration of the entire radiation dose.

It is interesting that the decrease of the scatter of data during slow (in comparison with acute) irradiation already was mentioned in a study by /212 Paterson (1944), who investigated the radiation reactions of a tissue culture in vitro. The author gave no analysis and explanation of this phenomenon. We found no other mention of such effects. There are no special investigations of the qualitative differences in the effect of acute and prolonged irradiations. We could find only individual random comments on this problem. Quastler et al. (1959) noted that the reaction to irradiation of the intestinal epithelium quantitatively and qualitatively depends on the irradiation dose intensity. Yu. I. Moskalev (1960) pointed out that in the case of injury by radioactive isotopes the irradiation intensity exerts an influence on lifetime and the blastmogenic effect in rats, both quantitatively and qualitatively. We observed a qualitatively different picture of the electrical resistance of the brain for different durations of irradiation (Apanasenko, 1961). /213

Vacek (1962), using mice, investigated the change of the general level of oxygen consumption after irradiation. With a dose intensity of 98 r/min the oxygen consumption increased to 140 percent, but with a dose intensity of 195 r/min it decreased to 60 percent. It is significant that the author mentions the important role of the CNS in the occurrence of this effect. After neurotomy of the spinal cord the oxygen consumption did not change, regardless of the irradiation dose intensities used. It is possible that the nerve system, sensing acute and prolonged irradiations as qualitatively different stimuli, is responsible for the occurrence of qualitatively different radiation reactions. The mechanism of both qualitative and quantitative influence of irradiation dose intensity on the response reactions of the body still is not entirely clear. There are numerous theories, hypotheses and explanations on the mechanism of the time factor effect, although the key role of the type of metabolism and repair process in some form is recognized by all radiobiologists (Luchnik, 1956; Aglintsev, 1960; Koznova, 1959; Nuzhdin et al., 1959; Domshlak et al., 1959; Strelin, Shmidt, 1957; Koznova, Khrushchev, 1960; Evans, Ellis et al., 1944; Mole, 1957; Lucille, Du Sault, 1956; Stearner, Tyler, 1957, 1962; Logie et al., 1960, and many others).

The key link determining the final effect of irradiation is the relation between the character of metabolism of a particular system and the radiant energy applied to it. The irradiated body may be regarded as a system of balance between the damaging and restorative processes (Maurer, Minder, 1960). A. V. Lebedinskiy and Yu. I. Moskalev (1960) proposed a rigorous discrimination between restorative processes proper (restoration of the initial irradiated structures) and the phenomenon of compensation of irreversibly impaired processes by other undamaged systems of the body. Such compensation apparently can be conceived of in the form of both morphological and functional replacement of the injured structure.

The balance between damage and restoration obviously will be different (in the case of single irradiation) for actively regenerating and nonregenerating tissues (Strelin, 1959). Differences can be expected both in the degree of the initial damage and in the final radiation effects. The initial damage of poorly regenerating tissues, which includes nerve tissue, can be less than in tissues with high mitotic activity. However, these tissues remain damaged for a

long time; the restoration processes in them are very slow. The total radiation dose is of the greatest importance here, not the intensity of the exposure. The "time factor" in such systems frequently exerts no influence on the result of the irradiation. However, it would be incorrect to speak of a /214 complete nondependence of radiation reactions of nonregenerating tissues on the irradiation time parameter. In the case of such tissues it is not impossible that there is functional compensation, the radiovulnerability of morphological structures possibly depending on the "time factor." In addition, there apparently are still some other possibilities for the exertion of a direct or inverse influence of the duration of exposure on the radiation effect in poorly regenerating tissue.

In particular, for an inverse dependence of radiation reactions of the nervous system on irradiation dose intensity it is possible to postulate the following.

1. A characteristic of the nervous system is its high functional activity. The greater radiosensitivity of actively functioning structures (Sokolova, 1962; and others) can be the cause of the inverse influence of the time factor on radiation reactions. With lengthening of the exposure there is an increase of the possibility of damage of alternately active functional units (Livshits, 1961).

Such an intensified vulnerability of the functioning neurons could be one of the causes for the increase of the effectiveness of prolonged irradiation on the vestibular reactions. Such mechanisms apparently also are manifested in the case of actively functioning mitochondria (Hug, Wolf, 1956) and in a number of other cases.

2. In the process of exposure there can be a change in the character of metabolism in the irradiated system. The end of the irradiation or the last fractional administrations of radiation may fall on a sensitized substrate and exert great damaging effect; prolonged irradiation is more effective. This type of change of the exchange of nucleoproteins is attributed by N. A. Poryadkova (1956) to the inverse influence of the time factor during the irradiation of germinating pea seeds. This phenomenon may also occur in the radiation reactions of the nervous system. However, metabolism also may change in the direction of greater radioresistance; then a small irradiation dose intensity is less harmful (Kallman, 1958; Stearner, Taylor, 1962; and others).

3. High irradiation dose intensity, under certain conditions, stimulates the protective forces of the body, that is, mobilizes its reserves. In this case acute irradiation may be less harmful (Strelin, Shmidt et al., 1957; Mole, 1959). The nervous system, with its broad capabilities of functional compensation, may well be characterized by such patterns of behavior (Livshits, Meyzerov, 1963).

4. V. N. Chernyshev (cited in Koznova, 1959) attributes the lesser effectiveness of large dose intensities (particularly in cases of brief exposures) to the process of recombination of ions and radicals. This process trans- /215pires more rapidly in cases of high ionization density which occur at the

time of more intense exposures. There are fewer free ions and radicals, and the chemical effect of the radiation decreases. In the case of small dose intensities, the value of recombination can be neglected; the effect is determined by the dose. In our case such a mechanism of greater effectiveness of prolonged irradiation could occur only to an insignificant degree, since we did not use high radiation intensities.

5. In addition to these mechanisms, the inverse influence of the time factor on radiation effects may be based on the functional properties of the nervous system itself.

For example, it can be postulated that prolonged exposure exhausts the nervous system to a greater degree; the periods of rests between exposures are shortened (Livshits, 1961). The principal nerve processes weaken and malfunctions of nervous activity are manifested more strongly.

In addition, it is not impossible that radiation of different intensity may be sensed by the nervous system as qualitatively different stimuli, which may cause quantitatively and qualitatively dissimilar responses. This hypothesis, which we expressed in 1961, in our opinion is confirmed by the results in this paper.

The summation of protective and conditioned inhibition (Lebedinskiy, Nakhil'nitskaya, 1960), intensifying the main neural processes, may exert a favorable influence on higher nervous activity in the early stages after irradiation. Under certain conditions this phenomenon may instead occur during the course of exposure to greater irradiation intensity.

At this time it is impossible to make a precise determination of the mechanism of the inverse influence of the time factor on the radiation reactions of the nervous system.

The effect probably is determined by the interaction of several mechanisms. The reactions of the nervous system to the effect of different stimuli (including irradiation) are exceedingly varied.

Some characteristics of these reactions should be based on the unusually high functional activity and flexibility of the nervous system.

With respect to the direction of the functional changes of the vestibular analyzer after irradiation, the results indicate a depression of the functions of the otolithic apparatus. In the presence of an appreciable qualitative difference in the dynamics of radiation effects, both prolonged and acute irradiation suppress the occurrence of vestibular-chronic reflexes to the muscles of the extremities. The muscular reaction to vestibular stimulation after prolonged irradiation weakens even to a greater degree than after acute irradiation; increases of electrical activity at the time of vestibular stimulation no longer occur; the electrical activity in the aftereffect of this stimulation is less; and the aftereffect itself was shorter than in the case of acute irradiation. The decrease of the function of the organ of equilibrium after prolonged irradiation has a stable and prolonged character. Our data

agree with the result of those authors who after irradiation discovered a decrease of the excitability and reactivity of the vestibular analyzer (Titov, 1957; Petelina, 1957; Grigor'yev, 1962; Sevan'kayev, 1963; Sveshnikov and Sevan'kayev, 1962).

It should be noted that the testing samples with which these authors worked (rotation with acceleration, caloric and other clinical tests) primarily involved the semicircular canals. The test which we used primarily caused stimulation of the otolithic apparatus. The labyrinth reflexes, which we encountered in our case, are related to the sensitive spots of the utricle (Magnus, 1924). The agreement of the results is an indication that both basic structures of the vestibular analyzer (otoliths and semicircular canals) change their functions in the same direction under the influence of penetrating radiation.

Contrary to the general character of the changes, there is an increase of the background electrical activity of the investigated muscles after prolonged irradiation. Analysis of this phenomenon involves special difficulties, since this reaction -- tonic stress of the muscles in a state of relative rest -- is simultaneously involved with several analyzing systems: motor, vestibular, proprioceptive, skin, etc. It is possible that the observed effect (increase of electrical activity of the muscles in a state of relative rest and decrease of the reaction to vestibular stimulation) is evidence of some differences in the direction of the radiation reactions on the part of different analyzers.

Summary

1. Prolonged irradiation of guinea pigs by Co^{60} in a dose of 500 r and dose intensity of 0.6 r/min causes a statistically reliable increase of the spontaneous electrical activity of the extensors of the rear extremity in a state of relative rest.
2. The bioelectric reaction of the indicated muscles, in response to adequate stimulation of the vestibular apparatus, decreases under the influence of prolonged irradiation. The latent period of this reaction increases and the aftereffect is greatly shortened.
3. All changes are statistically reliable and very prolonged. Normalization of the indices is noted only on the 25th-30th day after irradiation.
4. In most cases prolonged irradiation changes the investigated characteristics of the vestibular-tonic reflex to a greater degree than the same dose of acute irradiation (inverse influence of the "time factor").
5. The difference between the effects of acute and prolonged irradiations on the investigated parameters frequently is qualitative as well as quantitative. A different direction is observed in the effect of these forms of

irradiation (for example, background electrical activity, reaction to vestibular stimulation), and a special stability of effects is observed from the third-fifth day after prolonged exposure. The dispersion of the results in the case of prolonged irradiation is considerably less than the dispersion for acute irradiation.

6. According to hematological indices, the gravity of radiation sickness, and survival rate of the animals, prolonged irradiation is less effective than acute irradiation (direct influence of the "time factor").

COMBINED EFFECT OF DOUBLE EXPOSURE TO VIBRATION AND CHRONIC
IRRADIATION ON THE FUNCTIONAL STATE OF THE
VESTIBULAR APPARATUS

Z. I. Apanasenko

ABSTRACT

Guinea pigs were exposed to combined twofold vibration (15 min before and after irradiation) and prolonged gamma irradiation in a dose of 500 r and dose rate of 0.6 r/min. The bioelectric activity of the extensors of the rear extremities before, during and after adequate stimulation of the vestibular analyzer was studied. The survival rate, number of leukocytes in the peripheral blood, weight and general clinical state of the animals were investigated.

The effect of vibration changes the radiation effects on the electromyographic characteristics of the vestibular-tonic reflexes. These changes were most significant during the first days after the exposure. However, the effects of prolonged irradiation are less affected by vibration than the similar effects of acute irradiation. The number of cells in the peripheral blood, weight dynamics, general clinical state and survival rate of animals subjected to such combined exposure have no statistically significant difference from the corresponding parameters for prolonged irradiation alone.

The combined effect on the body exerted by irradiation and factors of a nonradiation character is discussed in rather numerous scientific investigations. However, in most cases a study has been made of the joint effect of irradiation and mechanical traumas, burns and loss of blood (Blinov, 1958; Aleksandrov et al., 1962; Gamaleya et al., 1959; Zurabashvili et al., 1958; Kovalenko, 1958; Kruk, 1960; Sokolov, 1956; Vargunina, 1962; Golubentsev and Shevyreva, 1960; Strelin, 1962; Suvorov, Saakov, 1960; Beloborodova et al., 1962; Bondina et al., 1958; Movsesyan, 1960; Pushnitsyna, 1957, 1962; Ryumina, 1962, and others). In a number of studies irradiation was combined with a state of shock, effect of an explosive wave, influence of high or low temperatures with a physical or functional load (Aleksandrova, Selivanova, 1963; Bondarenko, 1961; Vayl', Sarkisov, 1959; Il'inskaya, Astakhova, 1959; Kevleshvili et al., 1959; Markelov, 1961; Mushina, 1958; Popov et al., 1960; Topuriya et al., 1959, and others). These combined effects usually led to a mutual increase of the damaging effect of the several components. In

individual cases there was decrease of the damaging effect or more rapid normalization of the impaired functions. The basic data accumulated in the scientific literature on the combined effect of radiation and these nonradiation factors have been generalized in corresponding reviews (Khromov, 1959; Sokolova, 1962; Livshits, 1964, and others), and additional analysis is not required.

There has been inadequate study of the problem of the joint effect of irradiation and such dynamic factors as overloads and vibration. There are only a few studies on the combined influence of radiation and acceleration on a centrifuge or vibration on the living organism. Taylor (1960) investigated the joint effect exerted on a rat by irradiation in a dose of 600 r and 7 min acceleration on a centrifuge with acceleration of 20 g. The differences in the survival rate of the irradiated animals and the animals subjected to joint effects were not evident. Similar results were also obtained in another study, in which rats were subjected to acceleration on a centrifuge immediately /219 or 10 days after Co⁶⁰ irradiation (Lyle, 1961).

Acceleration on a centrifuge at the time of irradiation (Ivanov et al., 1962) led to an insignificant increase of the lifetime of the rats, in comparison with the lifetime of animals subjected only to irradiation (dose 1000 r). It was also noted that there was a difference in the number of leukocytes 5 min after exposure and later a relatively lesser decrease of weight in the animals subjected to combined factors.

With respect to the influence of vibration on radiation effects, until recently the only known study has been that of A. N. Ganshina (1961). On the basis of her investigations the author concludes that vibration considerably intensifies the pathomorphological effect of acute irradiation (400 r); the effect of fractional (100 r x 4) radiation is essentially the same. Recently a series of studies devoted to the joint effect of vibration and irradiation on some functions of the CNS have been carried out in the laboratory of N. N. Livshits. It was demonstrated that vibration considerably changes the influence of acute irradiation on oxidation processes in the brain tissue (Luk'yanova, 1964c), on the value of the latent period of the unconditioned passive defense motor reflex (Kuznetzova, 1964b) and on the functional state of the vestibular analyzer (Apanasenko, 1964b). Further development of this type of work is particularly important in connection with the successes of rocket technology and astronautics. Under space flight conditions vibration is one of the basic dynamic factors. The influence of this factor on the body (both separately and in combination with other agents) should be thoroughly studied. On the other hand, space flight imposes increased demands on the nervous system of the cosmonaut, and in particular, on the functioning of the vestibular analyzer.

We found no investigations of the combined effect of vibration and irradiation on the vestibular apparatus in the available literature. In our earlier study (Apanasenko, 1964b) it was demonstrated that under the joint influence of twofold vibration and acute irradiation (500 r) the influence of vibration frequently is dominant in the change of the functions of the vestibular

apparatus of guinea pigs. Vibration masks the damaging effect of radiation, sometimes right up to the very death of the animals.

It is known that the result of the joint effect of two factors on the living organism should depend on the dose and on the conditions of exposure to each factor.

The objective of our study in part was investigation of the joint effect on the vestibular apparatus exerted by twofold vibration and prolonged irradiation. It was established that a decrease of the intensity of the dose /220 of irradiation does not decrease, but frequently even increases the efficiency of the effect of radiation on the nervous system (Livshits, 1956, 1961, 1964; Meyzerov, 1964; Apanasenko, 1961). In this connection it is of interest to compare the effect of acute and prolonged irradiations in combination with an identical form of vibration. The possibility of such a comparison was ensured by the total identity of the remaining experimental conditions in the studies with acute and prolonged irradiations.

The experiments were conducted on male guinea pigs weighing 350-500 g. After stabilization of the values for the investigated parameters (10-15 days) the animals were subjected to a 15 min vibration with a frequency of 70 cps and an amplitude of 0.4 mm. After 20-30 min they were subjected to prolonged whole-body irradiation in a dose of 500 r with a dose intensity of 0.6 r/min, the duration of the exposure was 13 hr 54 min. Approximately 2-2.5 hr after the end of the irradiation the animals were subjected to repeated vibration under the same conditions as prior to irradiation. Further investigation of the animals was made 1, 2, 3, 5, 7, 10, 15, 20, 25 and 30 days after such combined exposure. The control guinea pigs were always investigated at the same times. The experimental group consisted of 12 animals; the control group consisted of 14. The functional state of the vestibular analyzer was evaluated on the basis of electromyographic characteristics of the vestibular-tonic reflex for the muscles of the rear extremities. The methods for recording the electromyograms, adequate stimulation of the equilibrium organ and processing of the results have already been described in the article on the influence of prolonged irradiation on the function of the vestibular analyzer (pp. 194-195).

In addition to the electromyographic investigation of the state of the equilibrium organ, allowance was made for the number of leukocytes in the peripheral blood, weight, body temperature, general clinical condition and survival rate of the animals.

As in the earlier studies, the variations of the values of all parameters prior to exposure did not exceed the limits of physiological normality.

The results of combined exposure on the characteristics of the vestibular-tonic reflex are analyzed on the basis of the mean integral values of the electrical activity of the investigated group of muscles. For comparative purposes, all figures show data on groups of animals subjected to the effect of vibration alone (15 guinea pigs) and prolonged irradiation alone (12 guinea pigs).

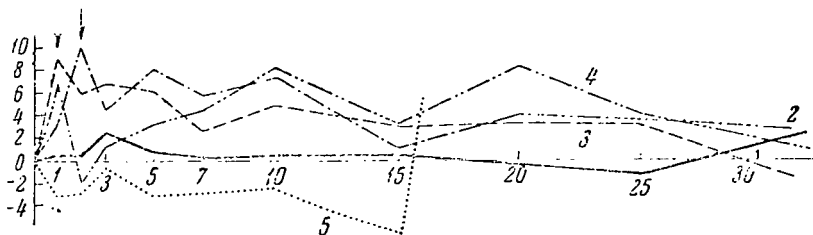


Figure 1. Change of background electrical activity of group of extensors of rear extremity (leg) after different types of exposure.

Along x-axis -- time after exposure in days. Along y-axis -- total electrical activity of muscles in percent of mean norm (on graph mean norm is assigned 0 value) and related to mean deviation for each group from norm prior to exposure. 1, Control; 2, group subjected to combined exposure; 3, vibrated group; 4, irradiated group; 5, curve for guinea pig which died. Arrows designate days of exposure.

In a state of relative rest (the animal is seated in a normal pose), the spontaneous bioelectric activity of the investigated muscles increases considerably after combined exposure (fig. 1). The changes were particularly significant during the first 10 days; by the 15th day after exposure the background electrical activity of the muscles decreases, but without reaching /221 the control level. On this day the value of the background myoelectric activity decreases in comparison with the tenth day in all animals of the experimental group. In half the animals the level of the muscular electrical activity decreases below the zero value. After the 15th day the spontaneous myoelectric activity again increases somewhat, and slowly decreases later, nevertheless remaining at a high level even a month after the combined exposure. The difference from the control was reliable both on the basis of the dispersion test ($P < 0.001$) and on the basis of the median test ($P < 0.001$). The median increases by 4.2 units and the dispersion increases greatly. The described character of the changes of the electrical activity of the investigated muscles in a state of relative rest was observed in all animals of this group, with one exception. The only guinea pig which died after the combined exposure (on the 16th day) up to the very time of its death revealed a steady decrease of the background myoelectric activity. Only on the day of the death did the spontaneous electrical activity increase greatly and considerably exceed the zero level (fig. 1).

In comparing the effect of joint exposure and the results of the separate effect of vibration and irradiation, there is a clearly discernible dominant influence of vibration in the combined effect during the first five days. In this period, during the joint exposure, the changes have the same direction and approximately the same order of magnitude as with vibration alone. After the fifth day the influence of vibration is already expressed to a somewhat lesser degree, although it still remains rather significant.

Beginning the tenth day the curves representing the effect of vibration and combined exposure are situated below the curve representing the effect /222 of prolonged irradiation alone. The values of the changes during combined exposure frequently occupy an intermediate position between the results of the separate effect of the individual components. On the fifth and seventh days after exposure the effects of the components seemingly are partially summed. On the second day, according to the literature (Ryumina, 1960; Suvorov, Saakov, 1960), there is the interesting phenomenon of intensification of the effect of one component and the opposite effect of the other. On this day the background electrical activity of the muscles increases after vibration, after irradiation it decreases somewhat, and after combined exposure it increases far more strongly than after vibration alone.

We note the fact of coincidence of the dynamics of changes during the combined exposure and during prolonged irradiation. Initially with a small time displacement, and then without it, the curve for combined exposure duplicates the shape of the curve of prolonged irradiation at a somewhat different level up to the 25th day. Being the result of the complex interaction of the effects of vibration and irradiation, the combined influence on the background electrical activity of the investigated muscles with respect to the dispersion test differs reliably from the separate influence of both vibration and irradiation (the dispersion increases, $P < 0.001$). With respect to the median test, no reliable differences are observed between the results of the compared types of exposure ($P > 0.05$), since the influence of both vibration and irradiation on the particular index is unambiguous, and the result of the combined exposure frequently occupies a median position between them. In this case the median increases by one unit in comparison with the effect of radiation and almost coincides with the median value of the vibration effect.

In a comparison of the two types of combined exposure (Apanasenko, 1964b) we note that the effect of prolonged irradiation changes somewhat less under the influence of vibration than the effect of acute irradiation. The dynamics of the changes conform fully to the influence of prolonged irradiation. The difference between the two types of combined exposure is statistically reliable on the basis of the dispersion test (for combination with prolonged irradiation the dispersion is greater $P < 0.001$) and is unreliable on the basis of the median test (the median for combination with prolonged irradiation is greater by 1.2 units $P > 0.05$). The electrical activity of the investigated muscles during the time of adequate stimulation of the equilibrium organ (fig. 2) decreases after combined exposure. Changes begin from the first day and with wavelike variations, persist to the 25th day after exposure. The effect is very stable and unambiguous for all animals of this group. Even for the guinea pig which died the changes had the same character, but were somewhat smaller in value than for the other animals. Difference from the control was reliable with respect to the median test ($P < 0.001$). After combined exposure the median decreases by 3.4 units in comparison with the control and by 4.2 units in comparison with the initial level. The value of the dispersion does not differ from the control ($P > 0.05$). /223

The illustration shows that on the first five days, as in the case of background electrical activity, the influence of vibration predominates in the effect of the combined exposure. In this period the purely radiation effect still

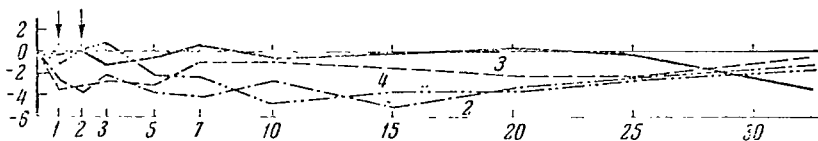


Figure 2. Change after different types of exposure observed in electrical activity of muscles at time of adequate stimulation of vestibular analyzer. Notations same as in fig. 1.

is not clear and the changes almost do not exceed the limits of the control. However, the curve for combined exposure almost merges with the curve reflecting the effect of vibration. However, by the seventh day the influence of radiation begins to be manifested more clearly in the combined effect. The curves of these two types of agents (joint and irradiation alone) approach and are then almost of the same shape, intertwining with one another in wavelike fashion. On the 25th day the effect of combined and separate exposure converge: a gradual return to normal begins. Here, as in a state of relative rest, there is a similarity of the dynamics of muscular electrical activity after irradiation alone and after combined exposure. Until the tenth day the curves of these agents have a very similar form; later the shape of the curves is duplicated, but with a time displacement. Thus, a clear influence of vibration on the radiation effect, with respect to this index, is observed only on the first five days after exposure. The result of the joint exposure differs reliably from the results of irradiation alone ($P < 0.05$ for the median test and $P < 0.001$ for the dispersion test) and vibration alone ($P < 0.001$ for the median test). In the combined exposure the median of the changes decreases by 1.3 units in comparison with the value of this index for vibration and by 0.9 unit for irradiation.

This indicates that the center of distribution of the changes after combined exposure is somewhat closer to this value after irradiation than after vibration.

As might be expected; the effect of combined exposure to vibration and prolonged irradiation differs from the effect of combined exposure to vibration and acute irradiation. In the latter case there is a relatively greater /224 nondependence on the influence of radiation. The greatest difference in the results of these two types of combined exposure occurs in the period from the second to the seventh day (Apanasenko, 1964b). In the case of the combined effect of vibration and prolonged irradiation (on the electrical activity of the muscles during vestibular irritation), the median of the changes decreases by 2.7 units in comparison with this index under the influence of a combination of vibration and acute irradiation ($P < 0.001$). The dispersion of the values of the changes in this case decreases by a factor of 6.3 ($P < 0.001$).

In the aftereffect of the myoelectric reaction to vestibular irritation (fig. 3) the electrical activity of the extensors of the rear extremities after a combined exposure also decreases. This decrease is not very great and



Figure 3. Changes after different types of exposure observed in electrical activity of muscles in aftereffect of reaction to adequate stimulation of the vestibular analyzer.

Notations same as in fig. 1.

has a wavelike character. The lowest level of electrical activity is attained by the 15th day; a gradual return to normal is observed after the 25th day. On the first day after exposure in three animals there was some increase of myoelectric activity in the aftereffect of the investigated vestibular-tonic reaction. Later the effect was the same for all animals. The difference from the control and from the initial data was statistically reliable ($P < 0.001$ for both tests). The median decreases by 2.6 units and the dispersion increases by a factor of 4.2.

Both the character of the changes in the aftereffect themselves and their relation to the effects of separate exposure to vibration and irradiation are very similar to those observed during the reaction to vestibular irritation. On the first three days the changes in this case also almost completely duplicate the vibration effects. However, already from the fifth day the influence of radiation begins to predominate in the effect of combined exposure. The effect of vibration still is appreciable and at times the effect of joint exposure seemingly approaches the vibration effect (10, 20 days), but on the whole the curve of the combined effect lies close to the curve representing the result of irradiation. The median of the changes during the combined exposure is situated 1.3 units lower than the median of the changes after vibration ($P < 0.01$) and only 0.4 unit higher than after a single irradiation ($P > 0.05$). According to the dispersion test the result of combined exposure differs reliably from the results of the separate effect of both components ($P < 0.001$). In the case of combined exposure the dispersion of values is twice as great as for irradiation alone and four times greater than for vibration alone.

Analysis of the collected data makes it possible to conclude that in the effect of combined exposure to vibration and prolonged irradiation the influence of radiation is manifested earlier and to a somewhat greater degree than in the effect of combined exposure to vibration and acute irradiation (Apanasenko, 1964b). The median of changes during the combination of vibration with prolonged irradiation is 2.2 units lower than in the case of combination of vibration with acute irradiation ($P < 0.001$). The dispersion of the values of the changes for both kinds of combined exposure is almost identical ($P > 0.05$).

Figure 4 shows the change of the latent period of myoelectric reaction in response to adequate irritation of the vestibular apparatus. After combined

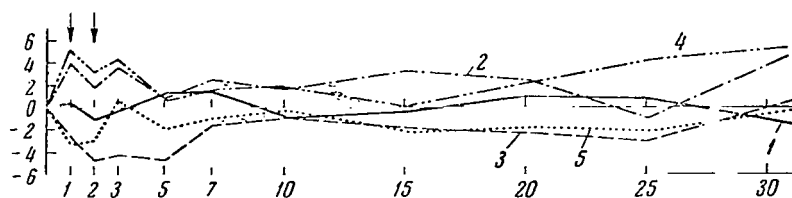


Figure 4. Change after different types of exposure observed in latent period of electromyographic reaction to adequate stimulation of vestibular analyzer. Along y-axis -- value of latent period in relative units. 5, Subgroup subjected to joint exposure (4 guinea pigs). Remaining notations same as in fig. 1.

exposure the latent period of this reaction is increased considerably during the entire period of observations (30 days). The changes have a wavelike character, but there is some decrease below the zero level only on the 25th day. There was no return to normalcy even 30 days after exposure. The maximum changes are observed on the first days after the exposure. The median of changes rises by 1.2 units above the control ($P < 0.05$); there is no significant change of dispersion ($P > 0.05$).

In comparison with the results of irradiation alone and vibration alone the influence of radiation in the effect of joint exposure is clearly apparent. The first 10 days the curve for combined exposure not only duplicates the shape of the curve of the results of irradiation, but almost merges with it. Later the curves diverge, but the result of joint exposure nevertheless remains closer (in sign and value) to the result of irradiation than to the result of vibration. The medians of the changes in the case of combined exposure and in the case of irradiation virtually coincide ($P > 0.05$). However, the median of changes during vibration lies 4.5 units lower ($P < 0.001$). According to the dispersion test the effect of combined exposure differs reliably from the effects of both vibration and irradiation ($P < 0.001$). In the first case the dispersion is considerably less than in the two latter cases.

However, the influence of vibration during combined exposure is also reflected in this parameter. First, the curve of combined exposure from time to time is displaced somewhat in the direction of the vibration effect. Second, with respect to change of the latent period, the vestibular-tonic reaction of the group of animals subjected to the combined exposure was varied. In 4 of the 12 guinea pigs the changes had a different character than in all other animals of the group (fig. 4). In these animals the latent period of myoelectric reaction to vestibular irritation after combined exposure for the most part decreased, as after vibration. On the first two days the decrease is rather considerable. On the following days the changes are less, but nevertheless exceed the limits of the control. The direction of the reaction in this case is the same as after vibration, although on the first seven days the effect is considerably less in its value. Beginning on the seventh day, the curve representing the

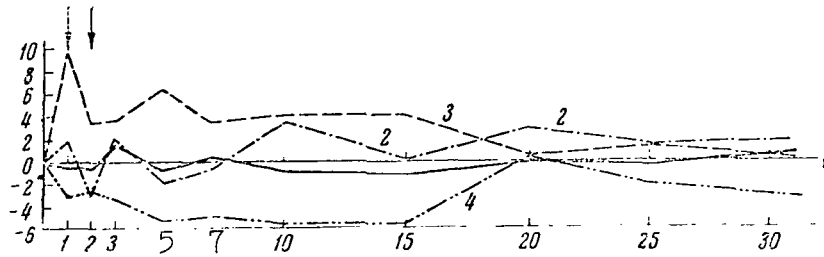


Figure 5. Change after different types of exposure observed in duration of aftereffect of electro-myographic reaction to adequate stimulation of vestibular analyzer.

Along y-axis -- duration of aftereffect in relative units. Remaining notations same as in fig. 1.

result of combined exposure for these animals approaches the curve representing vibration. Later both curves have a similar shape, being virtually identical.

Thus, with respect to this index, these four guinea pigs revealed a character of changes corresponding to the effect of vibration. The reaction of the other animals of the group indicated that the influence of radiation was greater.

In the case of combined exposure to vibration and acute irradiation the influence of radiation was manifested clearly only shortly prior to the death of the animals. A masking effect of vibration appeared in the early stages (Apanasenko, 1964b).

In the case of joint exposure to vibration and prolonged irradiation most of the animals reveal a reaction to the radiation influence from the very first days after exposure. The difference between the effects of the two types of combined exposure is statistically reliable with respect to the dispersion test ($P < 0.001$) and unreliable with respect to the median test ($P > 0.05$).

Rather rapid wavelike changes with transition through the zero level are characteristic for the duration of the aftereffect of the investigated /227 vestibular- tonic reaction (fig. 5) after combined exposure. The amplitude of the variations exceeds the limits of the control. After the 10th day the relative value of the duration of the aftereffect of this reaction no longer drops below zero; the variations continue to a higher level. After the 20th day there is a return toward normalcy, but complete normalization is not observed even on the 30th day. The median of the changes virtually coincides with the control ($P > 0.05$). The dispersion increases by a factor of 2.5 in comparison with the control and by a factor of 4.9 in comparison with the initial level ($P < 0.001$). In one guinea pig the duration of the aftereffect of myoelectric reaction at all times remained high; its value did not decrease beyond the zero level on even a single experimental day. In all remaining animals the changes were completely uniform.

In an analysis of the dynamics of the duration of the aftereffect of the reaction to vestibular stimulation after joint exposure we find a case when the effect of combined exposure of two influences opposite for a particular parameter occupies a mean position and sometimes even differs little from the control. Up to the 20th day the results of the separate influences of vibration and prolonged irradiation on the duration of the aftereffect are almost direct opposites. The value of the effect of combined exposure assimilates opposite influences and in this period of time varies near zero, shifting somewhat in the direction of the vibration effect. The median of the changes is 1.3 units above the median for irradiation alone and 1.1 unit below it for vibration alone. The dispersion of the values is 2.5 times greater than in the case of irradiation and 7 times less than in the case of vibration.

The effect of combined exposure with an equal degree of reliability differs both from the effect of vibration and from the effect of irradiation -- in both cases $P < 0.05$ for the median test and $P < 0.001$ for the dispersion test.

In this case different relations also appear than in the case of the combined effect of vibration and acute irradiation, where the dominating influences of vibration and irradiation seemingly were separated in time (Apanasenko, 1964b). The difference between the effects of the two types of combined exposure is reliable with respect to the dispersion test ($P < 0.001$) and with respect to the median test (P not much > 0.05) is on the boundary of reliability. In the case of joint exposure to vibration and prolonged irradiation the dispersion of the values is considerably less, and the median of the changes is situated 2.3 units higher than in the case of combined exposure to vibration and acute irradiation. Thus, in all considered cases the changes of myoelectric characteristics of the vestibular-tonic reflex in the case of combined exposure have clear indications of a vibration effect. This is manifested most clearly usually in the first period after exposure.

However, the clinical course of radiation sickness apparently does not conform to this pattern. Indications of the effect of vibration are virtually absent in this case. Thus, the dynamics of the number of leukocytes in the peripheral blood of animals after combined exposure do not differ essentially from the same after prolonged irradiation alone (fig. 6). In both cases there is a moderate decrease of the number of leukocytes (up to 1200-2300 per

mm^3). The maximum decrease is reached on the 7th-10th day; there is a gradual return to normalcy after the 20th day.

The difference from the control and the vibration effect is reliable ($P < 0.001$). No significant difference was discovered between the results of combined exposure and irradiation alone ($P > 0.05$). It is possible to note only a somewhat more rapid and smooth return to normalcy at the time of combined exposure.

There is an almost identical change of weight of animals after prolonged irradiation and combined exposure (fig. 7). In both cases an appreciable increase of weight begins with the third day and continues during the course of the entire experimental period. However, in both cases this increase does

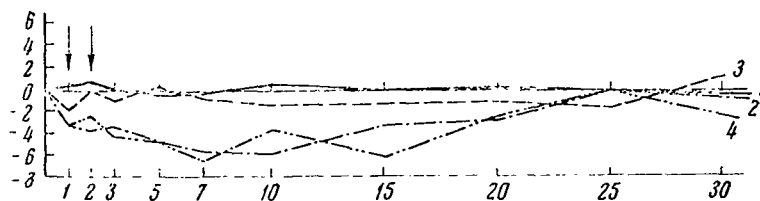


Figure 6. Change of number of leukocytes in peripheral blood of animals after different types of exposure.

Along y-axis -- number of leukocytes in 1 mm^3 of blood, expressed in percent of mean norm (on graph norm is assigned 0 value) and related to mean deviation for each group from norm prior to exposure. Remaining notations same as in fig. 1.

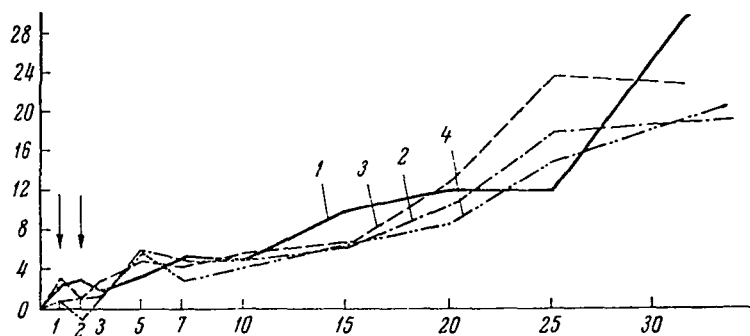


Figure 7. Change of weight of animals after different types of exposure.

Along y-axis -- weight expressed in percent of mean norm (0 on graph) and related to mean deviation for each group from norm prior to exposure. Remaining notations same as in fig. 1.

not differ reliably from the control ($P > 0.05$). The weight of the animals subjected to vibration alone changes in approximately the same way as in the case of irradiation and combined exposure. In this case it is therefore impossible to speak of a predominant role of any component in the combined effect.

The reliable difference between all four curves does not change ($P > 0.05$). In external appearance and general condition the animals after joint exposure did not differ from animals subjected to prolonged irradiation alone. In neither case did indications of acute radiation sickness appear. The relatively small number (12-16 per group) of experimental animals does not make it possible to draw reliable conclusions concerning the differences in the survival rate after combined exposure. No spontaneous losses occurred in the

control. There also was no death of animals after the separate effect of vibration and prolonged irradiation. After combined exposure to these factors one guinea pig died, constituting 8.3 percent of the number of animals in the particular group.

Thus, in the case of combined exposure to vibration and prolonged irradiation the investigated clinical indices (weight, number of leukocytes in the peripheral blood, general condition) were subjected to the effect of vibration to a still lesser degree than when vibration was combined with acute irradiation. Whereas in the second case the effects of the combined factors and irradiation alone diverge somewhat (during the joint exposure weight decreases more sharply and the number of leukocytes less sharply; the general condition is worse than in the case of irradiation), in the first case they are almost identical. The difference between the effects of the compared types of joint exposure with respect to the investigated clinical indices is statistically reliable ($P < 0.001$). This difference is determined by the completely different effect of acute and prolonged irradiations (with the same dose) on the clinical picture of radiation sickness and the survival rate of the animals. /230

Conclusion

On the basis of the results it can be concluded that double exposure to vibration exerts no appreciable influence on the survival rate of guinea pigs and clinical course of radiation sickness after whole-body prolonged gamma irradiation in a dose of 500 r. Information on the influence of vibration on the clinical state and survival rate of animals during irradiation could not be found in the literature. However, acceleration on a centrifuge usually either exerted no influence on survival rate in the case of irradiation (Taylor, 1960; Lyle, 1961) or caused an unreliable increase of the survival rate.

The radiation reactions of myoelectric characteristics of the vestibular-otonic reflex under the influence of vibration vary considerably. In the case of the vestibular analyzer vibration to a definite degree is an additional adequate irritant. It is known that a functional load on an organ in most cases causes an increase of its reaction to radiation (Sokolova, 1962; Vayl', Sarkisov, 1959; Sokolova, Gorshenina, 1960). The results obtained in this study for the reactions of the vestibular apparatus reveal more complex relations. In the case of a combined effect of vibration and prolonged irradiation it is possible to observe the following cases of interaction of the effects of the components.

Partial Summation of Effects in the Case of the One-Directional Effect of Vibration and Irradiation

Such an intensification of the radiation effect by exposure to vibration occurs for the background electrical activity on the 5th and 7th days and for

the electrical activity at the time of the vestibular-tonic reaction on the 5th, 7th and 15th days after exposure (figs. 1 and 2). These cases of incomplete summation can be considered as an aggravation of the radiation reaction under the influence of a nonradiation factor (vibration). Very many such examples are given in the literature (Blinov, 1958; Bondarenko, 1961; Markelov, 1961; Movsesyan, 1960; Movsesyan et al., 1962; Pashkovskiy, 1959; Strelin, 1962; Funshteyn, 1956, 1961; Tsverava et al., 1959; Shcherbina, 1962, and others).

Predominance of the Effect of One of the Combined Factors

Such a phenomenon is observed, for example, with a change of the latent period of myoelectric reaction to stimulation of the vestibular apparatus. /231 In the case of joint exposure in most of the animals the latent period of this reaction changes, as in the case of irradiation alone; in four animals the influence of vibration is predominant (fig. 4). A similar predominance of the vibration effect was also noted by M. A. Kuznetsova (1964b) in a study of the functional state of the reflex arc of the spinal reflex.

Combination of the Influence of Both Components in the Combined Exposure Effect

Very frequently the result of combined exposure on the first days is similar to the result of vibration alone, but in the later period it is similar to the result of irradiation alone (electroactivity of the muscles at rest, with time and in the aftereffect of the reaction to vestibular irritation -- figures 1, 2 and 3). Similar facts were observed in the case of the combined effect of radiation and burns by Sh. R. Topuriya and others (1959), by L. D. Luk'yanova (1964c) in an investigation of oxidation processes in cerebral tissue and by Clemenson and Nelson (1955) in a study of the joint effect of whole-body radiation and shock wave.

Partial or Total Nullification of the Effects of Components Directed in Opposite Directions

In this case the effect of combined exposure occupies an intermediate position between the effects of the separate influence of the individual components. There is a more or less considerable attenuation of radiation reactions. The result of the combined exposure in this case sometimes does not exceed the limits of the control. An example of the averaging of the effects of the components in this study is the dynamics of the duration of the aftereffect of the investigated vestibular-tonic reaction (fig. 5). Such data are also presented in the literature (Pushnitsyn, 1962; Kuznetsova, 1964b).

Interesting Phenomenon of Intensification of the Effect of One Factor Oppositely Directed to the Effects of the Other

Sometimes in this case there is appearance of effects of a completely different character, not observed for either of the individual components. Such an intensification of the radiation effect oppositely directed to the influences of vibration is noted, for example, for the change of background electrical activity on the second day, and for the change of the latent period -- on the 7th and 15th days after exposure (figs. 1 and 4). Similar phenomena were observed by V. A. Suvorov and B. A. Saakov (1960) in the case of burn shock after irradiation and by M. I. Ul'yanov and B. V. Sakharov (1963) in the case of combined radiation and moderate pain irritation. Ye. N. Ryumina (1962) mentions the appearance of leukopenia after combined bleeding (caused by leukocytosis) and internal irradiation (without a change of the number of leukocytes).

Thus, almost without changing the clinical state and survival rate of 232 the animals, vibration in the case of its joint effect with prolonged irradiation exerts an appreciable influence on the radiation reactions of the vestibular apparatus -- rear extremities extensors system. The difference in the efficiency of the influence of the nonradiation factor on the results of irradiation with respect to the different investigated parameters is described quite extensively in the literature (Mushina, 1958; Pinchuk, Shcherban', 1958; Sokolov, 1956).

The results of this work show that the effects of prolonged irradiation were subject to the influence of vibration to a somewhat lesser degree than the effects of the same dose of acute irradiation. In both cases of combined exposure there is complex interaction of the effects of vibration and irradiation. However, in the case of joint exposure to vibration and acute irradiation the influence of radiation is usually manifested later and is expressed somewhat more weakly than in the case of combined effect of vibration and prolonged irradiation (Apanasenko, 1964b). The effects of acute irradiation frequently were masked by the effects of vibration up to the time of the death of the animals. Guinea pigs subjected to combined exposure sometimes died despite indices corresponding to the control or a vibrated animal.

However, prolonged irradiation begins to dominate in the complex effect at an earlier time. It seemingly "draws" the result of the combined effect closer to itself. The curves representing the effect of prolonged irradiation alone and its effect in combination with vibration diverge considerably less than the corresponding curves for acute irradiation and its combination with the same vibration. Table 1 gives the median values of the differences between the mean relative effects of the combined exposure and irradiation. The table shows that in the series of experiments with acute irradiation the absolute values of the medians for almost all investigated indices are greater than in the series of experiments with prolonged irradiation. Only for the electrical activity of the muscles in the aftereffect of the vestibular-tonic reaction were the medians of the differences in both cases virtually identical. The lesser values of the medians of the differences between the values of the effects of combined exposure and prolonged irradiation alone (in comparison with these same

TABLE 1. VALUE OF MEDIANS OF DIFFERENCES BETWEEN RELATIVE EFFECTS OF COMBINED EXPOSURE AND CORRESPONDING FORM OF IRRADIATION

Investigated index	Series with acute irradiation	Series with prolonged irradiation	Reliability (P)
Background electrical activity of muscles	+8.89	+2.38	<0.05
Electrical activity of muscles at time of stimulation of vestibular analyzer	-11.17	-1.5	<0.01
Electrical activity of muscles in aftereffect of reaction to stimulation of vestibular analyzer	+0.1	-0.4	>0.05
Latent period of reaction to stimulation of vestibular analyzer	-1.09	-0.3	>0.05
Duration of aftereffect of reaction to stimulation of vestibular analyzer	+5.82	+4.47	>0.05

values in the series of experiments with acute irradiation) indicate that the curves for combined exposure and prolonged irradiation lie closer to one another than the corresponding curves in the series of experiments with acute irradiation. This difference is reliable with respect to the indices of electrical activity at rest and at the time of the reaction to adequate vestibular irritation. For the latent period and the duration of the aftereffect the difference of these medians is unreliable, but it can also be seen that the values of the medians of the differences in the experiments with acute irradiation are greater than in the experiments with prolonged irradiation. The 233 table thus confirms that in the case of combined exposure, the effects of prolonged irradiation change less under the influence of vibration than the effects of acute irradiation.

The lesser dependence on vibration influence can be attributed primarily to the fact that in the case of prolonged irradiation only a part of the radiation dose affects that functional background arising immediately after vibration. Furthermore, vibration in turn also corresponds only to the end of prolonged irradiation, e.g., with the last "portions" of it. Thus, in the case of prolonged exposure to radiation, somewhat different temporal relations with vibration are created than in the case of acute irradiation. However, the dependence of the combined effect on the relation of the factors operating with time is rather well known. The change of radiation effects under the influence of blood loss (Bondina et al., 1958), under the influence of a shock wave and electrical current (Zakharzhev et al., 1960; Popov, 1960; Hall et al., 1962)

and mechanical trauma (Kruk, 1960) depends on the time of application of these factors after irradiation.

The time of application of the nonradiation factor prior to irradiation also determines the overall effect of combined exposure (Bychkovskaya, 1955). However, there is some basis for assuming that the temporal relations between the components are not the only cause of the different effect of vibration on the effects of acute and prolonged irradiations. First, it was demonstrated that the effect of vibration on the investigated parameters persists for 7-15 and sometimes 25 days (Apanasenko, 1964a). Therefore, prolonged irradiation (with a duration of 14 hours) should coincide with period of consider- /234
able postvibration changes in the body. Second, it can be considered established that for the reactions of the nervous system in general, and the vestibular analyzer in particular (Z. I. Apanasenko), irradiations with a lesser dose intensity are more effective than acute irradiations. In this case the specific weight of radiation in the effect of combined exposure can increase. It therefore can be assumed that the factor directly responsible for the different effectiveness of vibration in combined exposure can be the radiation dose intensity. It is interesting that in this respect our data coincide with the results of the morphological investigations made by A. N. Ganshina (1961). She established that vibration intensifies the pathomorphological signs of radiation sickness in the case of acute irradiation (400 r) and exerts virtually no influence on them in the case of fractional irradiation (4×100 r). Essentially the same situation was discovered by A. D. Pushnitsyna (1962). In the case of a combined exposure the effect of blood loss was attenuated with a persistence of chronic irradiation up to 10 days (in comparison with 5 days initially).

The tests used in these studies were not related directly to the functions of the nervous system. However, these investigations reveal the possibility of a different influence of the nonradiation factor on the effects of different methods of irradiation (with the same dose).

In all probability, the lesser influence of vibration on the effect of prolonged irradiation depends both on incomplete identity (in comparison with the series of experiments with acute irradiation) of the temporal relation of the components of the combined agents and directly on the dose intensity of the irradiation.

Summary

1. The combined effect of double exposure to vibration and prolonged gamma irradiation in a dose of 500 r with dose intensity of 0.6 r/min causes a considerable increase of spontaneous electrical activity of the group of extensors in the rear extremities of the guinea pig in a state of relative rest.

2. The electrical activity of these muscles with time and in the aftereffect of the reaction to adequate vestibular stimulation decreases after combined exposure.

3. The latent period of the myoelectric reaction to adequate vestibular stimulation increases after combined exposure.

4. The duration of the aftereffect of this reaction in the case of combined vibration and prolonged irradiation undergoes wavelike variations at the zero level with some increase a week after exposure. /235

5. With respect to composition of the peripheral blood, dynamics of weight, general clinical state, and survival rate of the animals, no statistically reliable differences were discovered between combined exposure and the effect of prolonged irradiation alone.

6. In the case of combined exposure to vibration and prolonged gamma irradiation, vibration more or less significantly changes the effect of radiation on the electromyographic characteristics of the vestibular-tonic reflex.

Most frequently the influence of vibration predominates in the effect of combined exposures in the early stages while the influence of radiation predominates in the late stages. Occasionally, some of the animals in the course of the entire period of observations reveal a predominance of the influence of vibration and the others--the influence of radiation. Sometimes oppositely directed effects of the components nullify each other and the result of combined exposure does not differ from the control.

7. The effects of prolonged irradiation change under the influence of vibration to a somewhat lesser degree than the corresponding effects of acute irradiation.

COMBINED EFFECT OF VIBRATION AND IONIZING RADIATIONS
ON THE CONDITIONED REFLEXES OF RATS

N. N. Livshits and Ye. S. Meyzerov

ABSTRACT

Groups of rats were exposed to:

I. Combined effect of whole-body vertical vibration at 70 cps and an amplitude of 0.4 mm for 15 min and immediately afterwards to total X-irradiation (50 r).

II. Effect of vibrostand noise for 15 min and then to total X-irradiation (50 rad).

III. Effect of vibrostand noise for 15 min (control).

All exposures were repeated three times. The interval between the first and second exposures was 14 days and between the second and third was 7 days. Experiments on rats exposed to vibration only were used for comparison. These were described in another paper by these same authors.

Conditioned motor alimentary reflexes in rats were studied.

In the first week after the first combined exposure the vibration effect dominated with respect to all indices. In the second week after the first exposure the combination of the effects of both factors was noted.

After the second and third combined exposures the effects of irradiation and vibration were completely summed.

Many published studies deal with the combined effect of ionizing radiations and factors of a nonradiation character. It is shown that a combination of irradiations and the effect of other factors can complexly change not only the quantitative characteristics, but also the direction of radiation reactions. This problem was considered in a review article published earlier (Livshits, 1964). The joint effect of vibration and irradiation has been investigated only recently due to the new importance of this problem for space biology and medicine. /236

It was established that the preliminary, and in some studies, also subsequent exposure to vibration can change many radiation reactions

(Ganshina, 1961; Antipov et al., 1963; Arsen'yeva¹; Demin, 1964; Parin et al., 1965).

The studies conducted by our group demonstrated that under the influence of vibration there is an appreciable change of the reaction of different parts of the CNS to irradiation (Apanasenko, 1964b; Apanasenko, Kuznetsov, 1964; Kuznetsova, 1964b; Lukyanova, 1963, 1964c). Investigations of the combined effect of vibration and ionizing radiations on higher nervous activity could not be found in the available literature. Our objective was study of this problem.

Data and Method

The experiments were carried out with mature male Wistar rats. At the beginning of the experiment the rats were 12-14 months old. The method for investigating the conditioned reflexes and preparing the animals was described in our preceding article in this collection.

The rats were divided into two equal groups. One group was subjected /237 to the effect of whole-body vertical vibration with a frequency of 70 cps, amplitude of 0.4 mm, and duration of 15 min and soon after this to X-irradiation in a dose of 50 r under the following conditions: RUP-11 apparatus, 200 kV, filters of Cu 0.5 mm: Al 0.75 mm, skin-focal length 49 cm, duration of exposure 1.5 min. The rats of the other group were irradiated in the same dose under these same conditions. Prior to irradiation, for a period of 15 min they were near an operating vibrating apparatus which was accompanied by a noise with an intensity of about 75 db. The control rats were situated near the operating vibrating apparatus for 15 min and then were placed in an X-irradiation chamber, but were not irradiated. There were three exposures: the pause between the first and second exposures was 14 days, and the interruption between the second and third exposures was 7 days.

Half the rats used in both the experimental and control groups were characterized before the exposure by a high level of conditioned reflexes with correct intensity relations, absolute differentiations, absence of extinction of conditioned reflexes and a stable, conditioned reflex background. In the remaining rats the mean level of conditioned reflexes was somewhat lower; there were cases of the extinction of conditioned reflexes and phase phenomena, most frequently at a low level, the differentiations in large part were relative and the conditioned reflex background was not entirely stable. Testing with daily starvation and extinction and restoration of the conditioned reflex were withstood by all rats to the same degree.

¹Reference is to an article in: G. M. Frank, N. N. Livshits, M. A. Arsen'yeva, Z. I. Apanasenko, M. A. Kuznetsova, L. D. Luk'yanova and Ye. S. Meyzerov. Influence of Space Flight Factors on Some Body Functions (Vliyaniye faktorov kosmicheskogo poleta na nekotoryye funktsii organizma) (in press).

The similarity of the makeup of the rats in the groups was ensured by the fact that each rat subjected to the joint exposure had a partner with similar indices of higher nervous activity in the irradiated group.

Prior to the experiment the experimental animals were used as controls. Prior to the end of the investigation it was possible to use only eight rats in each group; the results of experiments on these rats were used for statistical processing.

In addition to the principal groups of animals, four rats were subjected to the exposure; their partners died from random illnesses at different stages of the work. The data obtained with these rats were not included in the statistical processing and are described separately.

Results of Investigations

During the entire period of the investigations the experimental and control rats remained in good condition and were active.

During and after the experiment the average weight of the rats in all groups remained constant (table 1).

In order to avoid an influence on the conditioned reflexes by the procedure of taking blood samples, the hematological indices of the other groups of rats were investigated after they had been subjected to the same factors as the principal experimental groups. /238

The content of leukocytes in the peripheral blood of rats subjected to irradiation and combined factors decreased by 20-50 percent, compared with the initial level. The individual variability of the leukopenic reaction was so great that it was not possible to detect differences between the groups on the basis of our data.

In this series of experiments the changes of the conditioned reflex activity in the control group were expressed very weakly. After the first exposure there was an insignificant and statistically unreliable decrease of the intensity of conditioned reflexes to both irritants by 3-7 percent, compared with the initial level. Later the intensity of these reflexes exceeded the initial level by 10 percent and fluctuated near it, varying by ± 15 percent (figs. 1 and 2).

We will explain this absence in the principal groups of rats of the "August" line, whose conditioned reflex background was the least stable.

The effect of whole-body X-irradiation in the doses which we used on the conditioned reflexes of rats was investigated in detail on the basis of extensive data obtained by L. I. Kotlyarevskiy and his associates (1956; 1958a,b).

TABLE 1. WEIGHT OF RATS IN PERCENT OF INITIAL BACKGROUND.

Exposures to which rats were subjected	I Expo- sure	II Week after expo- sure	II Expo- sure	III Expo- sure	I Week	II Week	III Week
					After exposure		
Vibration and irradiation	102.1	104.2	102.8	103.7	104.7	105.1	104.4
Irradiation	101.9	104.0	104.0	103.8	102.1	106.5	105.5
Control	102.3	102.1	103.8	105.7	106.8	-	-

They demonstrated that radiation effects in these doses cause clear changes of conditioned reflex activity. Both the value of the reaction to irradiation and its direction are variable and depend on the type of higher nervous activity of the animal.

In our experiments the effects of irradiation were essentially close to those described by these authors. We found it more difficult to establish the dependence between the type of higher nervous activity and the reaction to irradiation due to the small number of animals and the absence of a full investigation of the type; therefore here, as in the preceding article, we consider it more proper to speak of individual rather than typological differences.

After the first irradiation there was an increase of the mean total /239 intensity of the conditioned reflexes in most (six of eight) rats (fig. 1). In this case the positive conditioned reflex to tone (tone+) increased, and the reflex to light decreased insignificantly (fig. 2). Therefore, the proper relationships between the intensity of the irritant and the value of the reaction during the first week after irradiation not only persisted, but became still clearer than before irradiation.

A decrease of the intensity of the conditioned reflexes was observed in only two rats. In one of them the reactions decreased to both irritants, and in the second only to light. The differentiation among the irradiated rats not only was maintained, but intensified considerably (fig. 3), despite an increase of the conditioned reflex coupled to it. In the second week after irradiation the conditioned reflexes began to decrease; in four rats (Nos. 18, 8, 7, 11) their values fell below the initial level. The resulting curve in this period also passes below the initial level. The number of experiments in which phase phenomena were observed did not increase, but the averaged data show that the conditioned reflex to a strong irritant tone+ suffered more /240 than the conditioned reflex to weak light (fig. 2).

The differentiations in this group remained intact (fig. 3). In most (six of eight) of the rats the reaction to differentiation decreased. In the two

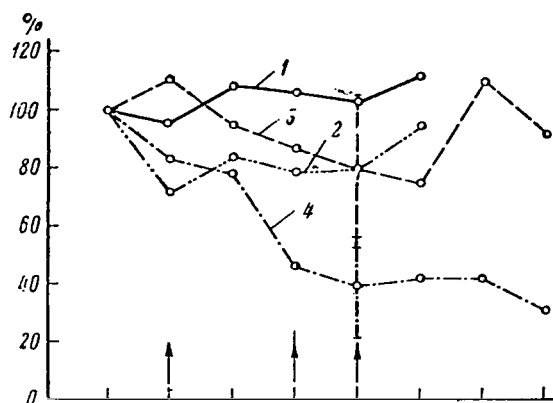


Figure 1. Influence of irradiation, vibration and combined exposure of vibration and irradiation on total intensity of conditioned reflexes.

Along x-axis -- time in weeks. Along y-axis -- mean group changes of particular index, expressed in percent in relation to mean initial level. The arrows denote the days of exposure. 1, control rats; 2, group of rats subjected to vibration; 3, irradiated group of rats; 4, group of rats exposed to vibration with subsequent irradiation. Vertical lines on the curves represent mean error multiplied by "t" with $P < 0.05$.

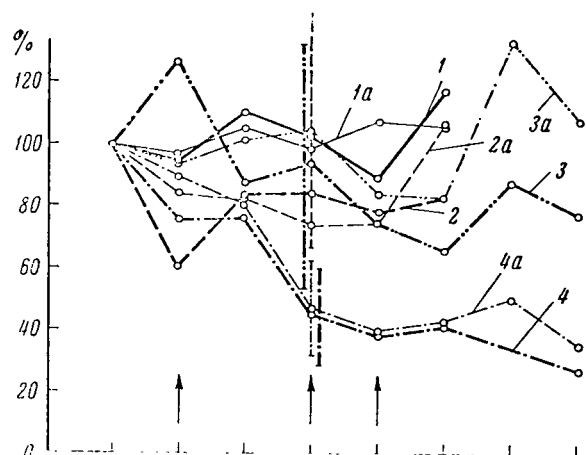


Figure 2. Influence of irradiation, vibration and combined exposure to vibration and irradiation on intensity of conditioned reflexes in response to strong and weak positive stimuli.

1, 2, 3, 4, conditioned reflexes to strong stimulus (tone+); 1a, 2a, 3a, 4a, conditioned reflexes to weak stimulus (light). Remaining notations same as in fig. 1.

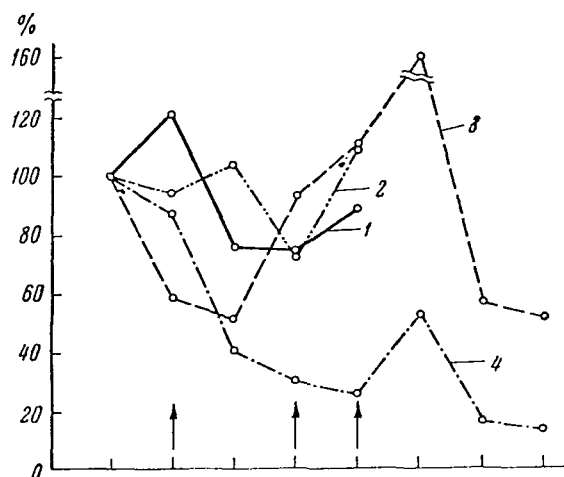


Figure 3. Influence of irradiation, vibration and combined exposure to vibration and irradiation on differentiated inhibition.

Along y-axis -- reaction to differentiation (tone-), expressed in percent of mean initial level. Remaining notations same as in fig. 1.

rats in which the reaction to differentiation was intensified the ratio of the value of the reaction to differentiation to the reaction to the positive irritant paired with it (index $\frac{\text{tone-}}{\text{tone+}}$) nevertheless decreased.

As was demonstrated in the preceding article, the effect of the first exposure to vibration was directly opposite. For convenience in comparison these data were plotted in figures 1, 2 and 3. After the first vibration the conditioned reflexes for both irritants decreased. The maximum changes were discovered in the conditioned reflex to a strong irritant, in which a tendency to impairment of correct intensity relations was manifested. The mean value of the reflex to differentiation decreased, but a disinhibition of differentiation was observed in individual cases in those of the rats with least expressed decrease of positive conditions.

In the second week after exposure to vibration the conditioned reflexes increased, without reaching the initial level, and since at this time the intensity of the conditioned reflexes in the irradiated rats had decreased, the mean values of the group indices converged. In the group subjected to combined exposure, after the first exposure the vibration effects predominated completely.

The conditioned reflex to tone+ decreased in seven of the eight rats and only in one was there an insignificant increase. The conditioned reflex to light suffered to a lesser degree; its intensity decreased in only five rats, but the mean group value was lower than the initial level. A tendency to

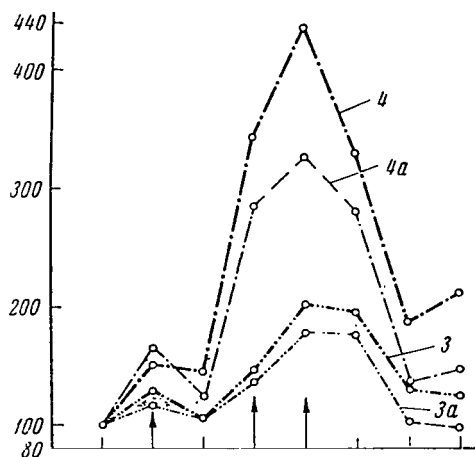


Figure 4. Influence of irradiation, vibration and combined exposure to vibration and irradiation on latent periods of conditioned reflexes. Notations same as in figs. 1 and 2.

disruption of the proper intensity relations, as in the vibrated group, is clearly seen from the averaged data in figure 2. The dynamics of the changes of the latent periods of the conditioned reflexes are shown in figure 4.

The decrease of the intensity of the reflex to tone+ after joint exposure was less clearly expressed than after vibration. However, quantitative comparison of the reactions of these groups was impossible, because their makeup was dissimilar. A rigorous identity of makeup was ensured in the groups subjected to irradiation and joint exposure, which we will compare statistically.

In five of the eight animals subjected to the joint exposure the index $\frac{\text{tone-}}{\text{tone+}}$ increased. In four cases this also was accompanied by an increase of the absolute value of the reaction to differentiation. In four of the five rats with disrupted differentiations, the positive reflexes suffered to a lesser degree. Due to the dissimilarity of the results, these data, as in the group subjected to vibration, were unreliable. However, the similarities between effects of joint exposure and vibration for this index cannot easily be considered random.

In the second week after the first irradiation, when the conditioned reflexes to tone+ in the vibrated rats began to be restored, but decreased in the irradiated rats, the group values of these indices decreased. In rats subjected to joint exposure the mean intensity of the conditioned reflex to tone+ remained the same as in the first week after the exposure.

The dynamics of the changes of this index occupied an intermediate position between the direction of the effects in the irradiated and vibrated rats,

but the value of the changes relative to the initial level was greater than under the influence of each of these factors separately. As can be seen from figure 2, the mean group differences according to this index still were small and obviously unreliable, but in the subsequent stages of the investigation they were intensified.

The conditioned reflex to light in rats subjected to combined exposure decreased somewhat, and its changes were considerably closer to those for the vibrated animals than in the irradiated animals. Thus, the total domination of the vibration effects in the course of the first week after joint exposure was replaced in the second week by a combination of the effect of vibration and irradiation characterized by partial, temporarily incomplete and unreliable summation. /243

After the second irradiation the conditioned reflexes in six of the eight rats fell below the initial level; in one rat (No. 7), in which the conditioned reflexes earlier had increased, they returned to the initial level. The insignificant decrease of the mean values of the conditioned reflex to tone+ can be attributed to a sharp increase of this index in only one rat (No. 12). Due to the great scatter, the position of this point is not reliable. The conditioned reflex to light suffered less than the reflex to tone and the tendency to a disruption of force relationships, which can be seen in figure 2, although the number of experiments with obvious phase phenomena was not increased. In three rats there was a small disinhibition of differentiations with an increase of the index $\frac{\text{tone-}}{\text{tone+}}$.

The third irradiation caused further attenuation of the stimulation process. The conditioned reflexes to tone+ were considerably lower than the initial level in seven of the eight rats, and in only one rat (No. 12) did the reflex increase.

The conditioned reflexes to light suffered somewhat less. After the second irradiation they decreased in five, while after the third, in six rats. The mean decrease of the intensity of the reflex to light was less clearly expressed than the decrease of the reflex to tone. Differentiation was disrupted in two rats.

Figure 2 shows that at this stage the conditioned reflexes decreased both under the influence of vibration and under the influence of irradiation. The differences were that in the irradiated animals the conditioned reflexes suffered more from strong stimuli, while in the vibrated animals, more from weak stimuli.

After the second and third joint exposures the decrease of conditioned reflexes was far sharper than in the case of separate application of vibration and irradiation, and the difference was reliable according to Student's test both for the mean total intensity of the conditioned reflexes and for reflexes to tone+ and light ($P < 0.05$).

In this group the conditioned reflexes to both stimuli decreased below the initial level in all rats without exception, and the decrease was more

considerable than in the irradiated animals. The changes of latent periods of conditioned reflexes were also sharper (fig. 4).

Quantitative comparison of the effects of combined and vibration expo-^{/244}sure is impossible for the reasons mentioned above, but there is no basis for considering our data on the effect of vibration to be understated. In the group subjected to vibration, there were two "August" rats which in reactions to vibration considerably exceeded the reactions in rats of the "Wistar" line used in this study. In addition, as demonstrated by the control experiments, the "Wistar" rats were also less sensitive to noise, and therefore we can assume that the effect of combined exposure in any case was not less than the sum of the effects of irradiation and vibration.

The reactions to differentiation in this group decreased considerably in six of the eight rats, which probably was related to a sharp decrease of the conditioned reflex to a positive stimulus. The small differentiation disinhibition in two rats was accompanied only by an increase of the index

$\frac{\text{tone-}}{\text{tone+}}$. The mean group indices of the reaction to differentiation in rats subjected to joint exposure was lower than in irradiated rats. This can be related to the summing of conditioned inhibition, with a protective inhibition more clearly expressed in the first.

The relations of the reflexes to weak and strong stimuli in rats after the second and third combined exposures occupied an intermediate position between the changes of these indices in irradiated and vibrated animals. After irradiation at these stages there is a greater disruption of the conditioned reflex to a strong stimulus, and after application of vibration -- the conditioned reflex to a weak stimulus. After joint exposure the intensity of both reflexes decreased in relation to the initial level to an equal degree.

Although on the graph for averaged data in this group there is an insignificant disruption of force relationships, the number of obvious phase phenomena at a low level in this period increased reliably in comparison with the initial background.

We expressed the number of phase phenomena in percent to the number of present conditioned reflexes, because the extinction of conditioned reflexes at this time was observed frequently and it was necessary to take them into account.

As pointed out in the preceding article, in the vibrated rats there was also an increase of the number of phase phenomena. However, in this case reliable changes were observed only in the statistical processing of the composite data after all exposures.

In the irradiated animals both conditioned reflexes decreased uniformly in all experiments, with less clearly expressed disruption of the reaction to the weaker stimulus. However, the ratio of the number of obvious phase phenomena to the number of present conditioned reflexes remained virtually unchanged ^{/245}(fig. 5).

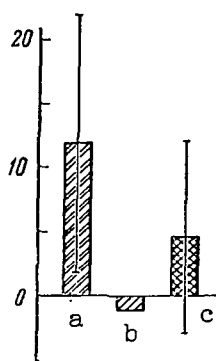


Figure 5. Number of phase phenomena after second and third exposures to irradiation, vibration and vibration with subsequent irradiation.

Along y-axis -- number of phase phenomena at low level, expressed in percent of number of conditioned reflexes present.
a, Combined effect of vibration and subsequent irradiation; b, irradiation; c, vibration.
Vertical lines on bars represent mean errors multiplied by "t" with $P < 0.01$.

Beginning with the third week after the end of the exposure in the rats subjected to vibration with subsequent irradiation, the relative intensity of the conditioned reflex to light, with respect to averaged data, exceeded the conditioned reflex to tone, but the differences between the experimental groups in this case were not smoothed and increased still more (fig. 2). Only beginning with the fifth week after the end of exposure were the conditioned reflexes to tone comparable in both experimental groups, not attaining the initial level. Data obtained later than the fourth week after ending of exposure should be checked, since by this time some of the rats had died from random illnesses and the number of remaining rats was inadequate for statistical processing.

At all stages of the investigation during the time of exposure and in the four-week period after termination of exposure the disruptions of the conditioned reflex activity in rats subjected to combined exposure were more severe than in the irradiated group.

Summary data on the differences of changes of the values of conditioned reflexes in the groups of rats subjected to irradiation and the effect of vibration with subsequent irradiation are given in table 2.

Although at some stages the disruptions of force relationships in the irradiated rats were more clearly expressed, we believe that combined exposure caused a sharper protective inhibition than irradiation. In rats subjected to

TABLE 2. DIFFERENCES IN CHANGES OF CONDITIONED REFLEXES IN RATS SUBJECTED TO IRRADIATION AND COMBINED EFFECT OF VIBRATION AND IRRADIATION.

Investigated index of higher nervous activity	Degree of change of particular index		
	Irradiated rats	Rats subjected to combined exposure	P, according to median test
Decrease of mean total intensity of conditioned reflexes	Less than	More than	<0.01
Decrease of mean intensity of conditioned reflex to tone+	Less than	More than	<0.05
Decrease of mean intensity of conditioned reflex to light	Less than	More than	<0.01

joint exposure, the level of the conditioned reflexes to both stimuli always was very much lower than in the irradiated group, and therefore their higher nervous activity was closer to the inhibition phase.

In addition to the principal groups, four other rats were subjected to exposure; the results of experiments on these rats were not included in the statistic processing. One rat (No. 16) differed sharply from our other experimental animals with respect to the indices of the initial level. In this case there were no positive conditioned reflexes. During the last two weeks prior to the exposure, 79 percent of the conditioned reflexes disappeared ^{/246} in this rat. Despite such low-level conditioned reflexes, the differentiations were not absolute. In contrast to rat No. 4, described in the preceding article, in rat No. 16 starvation did not cause a decrease, but instead an increase of the conditioned reflexes with disinhibition of differentiations, and noise (presence near an operating vibrating apparatus for 15 min) exerted no significant influence on the conditioned reflexes. This rat was subjected to the combined effect of irradiation and vibration. In this rat the effects caused a sharp increase of conditioned reflexes and disinhibition of differentiations, later replaced by a decrease of these reflexes below the initial level (figs. 6 and 7). Due to the absence of a partner for this rat in the irradiated group, we did not include the experimental results for this animal in the statistical processing.

We also prepared three pairs of "August" rats for exposure. However, ^{/247} in each pair one rat died of different illnesses in the early stages of the work, and the remaining living animals differed so sharply from one another with respect to the indices of higher nervous activity that they could not be partners. One of these rats (2) was subjected to irradiation and two (15 and 19) were exposed to the combined factors. The results of experiments on rats Nos. 2 and 19 were similar to those observed for rats of the corresponding

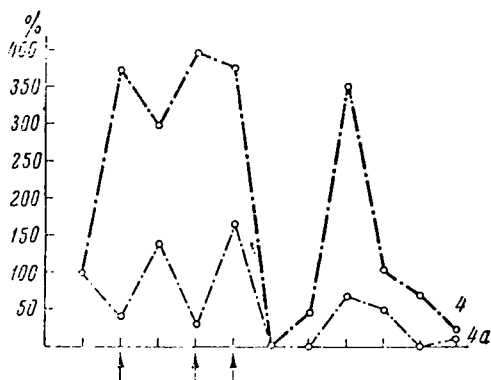


Figure 6. Influence of combined exposure to vibration and irradiation on conditioned reflexes of rat No. 16. Notations same as in fig. 2.

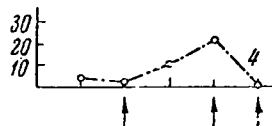


Figure 7. Influence of combined exposure to vibration and irradiation on differentiated inhibition of rat No. 16. Notations same as in fig. 3.

principal groups. In rat No. 15 the combined exposure caused a sharp increase of conditioned reflexes in all stages of the investigation. The conditioned reflex background for this rat was unstable, but the level of conditioned reflexes at normal for this rat was not lower than for rat No. 19.

These experiments show that an extremely significant increase of conditioned reflexes also is possible in the case of combined exposure, but if the identity of the makeup of the compared groups is ensured, the decrease of the conditioned reflexes is more clearly expressed after combined exposure than after irradiation alone.

Although the exclusion from the statistical processing of the data obtained for these rats was completely justified, we decided to check, nevertheless, what influence on the averaged data would be exerted by including the experiments with these rats. For this purpose we combined the results of the experiments on the "August" and "Wistar" rats and processed them statistically. With such grouping the conditioned reflexes for the rats subjected to the combined exposure were lower according to the medial test than in the irradiated rats ($P < 0.05$).

Discussion

In the rats subjected to combined factors in the six days after the first exposure there was complete dominance of the vibration effect. The similarity between the changes of the conditioned reflex activity in rats subjected to joint exposure and vibration alone was manifested with respect to all indices.

Beginning with the second week after exposure the combination of effects of the radiation and dynamic factors became complex. In the combined exposure, according to a number of indices, the phenomena of summation of the effects of both factors and their interference began to appear.

The dominance of the vibration effect in the early period after combined exposure has already been described by the specialists of our group. This phenomenon was observed in very clear form in an investigation of the effect of vibration and irradiation in lethal doses on the content and rate of /248 utilization of oxygen in the tissues of the brain and some indices of the vestibular-tonic reflex. Our experiments show that this pattern of behavior is general not only for oxidation metabolism of the brain and lower nervous activity, but also for the higher nervous functions. This reaction is manifested in the case of combination of vibration with fatal irradiations (Apanasenko, 1964b; Luk'yanova, 1963, 1964c) and with irradiation in relatively small doses (our experiments). The considerable decrease of dose intensity also does not introduce essential changes in the direction of this effect (Z. I. Apanasenko, p. 21). Nevertheless, such a form of reaction is not universal.

In the changes of the defensive unconditioned reflexes under the influence of vibration with subsequent gamma irradiation in a dose of 600 r in one group of guinea pigs there was dominance of the vibration effect, while in the other dominance of the radiation effect (Kuznetsova, 1964b).

We observed a different picture after repeated combined exposure. According to the principal indices of higher nervous activity -- intensity and latent period of the conditioned reflexes -- the vibration and radiation effects were completely summed. The dominance of the vibration effect was manifested only in an increase of the number of phase phenomena. Our data differ from the experimental results of A. N. Ganshina (1961). During combined vibration and fractional irradiation this investigator found no summation of structural changes, which was clearly expressed in the case of a single exposure. Possibly the reason for the discrepancies in the results was the dissimilarity of the exposure conditions. A. N. Ganshina used a four-hour vibration period, during which adaptation could develop sooner than in our experiments.

Under our conditions with triple exposure to vibration, adaptation phenomena did not arise. This was demonstrated not only in our experiments, but also in the articles by L. D. Luk'yanova et al. and M. A. Kuznetsova in this book.

In the case of a single exposure, the summation of the effects of the individual factors has not been observed until now in such obvious form. Despite the fact that both vibration and irradiation caused a depression of oxidation processes in the brain tissues, no summation of effects occurred. Moreover, at some times the effect of combined exposure was less than for exposure to radiation alone.

L. D. Luk'yanova (1964c) regards this as a manifestation of the protective effect of depression of oxidation processes and protective inhibition caused by the vibration factor in the higher parts of the brain. These data agree

very well with the results of the investigations of M. A. Arsen'yeva¹ and /249 Yu. S. Demin (1964).

Yu. S. Demin did not find a summation of the effects of vibration and irradiation in the frequency of mitoses in the cell nuclei of the bone marrow of mice, although each of these factors separately caused an increase of the number of impaired mitoses.

M. A. Arsen'yeva noted that after exposure to vibration and subsequent irradiation with 350 r the frequency of the true chromosomal aberrations was lower than after irradiation with this same dose. It is therefore extremely probable that the reactions described by L. D. Luk'yanova, M. A. Arsen'yeva and Yu. S. Demin have similar mechanisms.

In our experiments with repeated exposures there was no manifestation of a defensive effect of protective inhibition, although it would seem that its influence should be reflected primarily in conditioned reflex activity. It was difficult to say whether the defensive effect of protective inhibition was masked by the opposite effect of other factors, or whether it was absent because the problem of the dependence of the radioresistance of the CNS on its functional state still has not been solved with certainty. Increased functional activity intensifies the radiovulnerability of the CNS (Sokolova, 1962). There is also an intensification of the radiovulnerability of functional traumatism of the CNS (Kurtsin, 1958). There are no specific experimental data on the problem of what relation of stimulating and inhibiting processes in the higher parts of the CNS is optimal for creating radioresistance.

The radiodefensive effect of a depression of oxidation processes is widely known, and its effect has been well studied at different levels of organization of living subjects.

As was demonstrated in the preceding paper, the effects of vibration on the conditioned reflexes after the first and subsequent exposures did not differ appreciably from one another. The influence of this factor on oxidation processes in the brain tissues also was virtually identical in the course of the first three applications (Luk'yanova, 1964b; L. D. Luk'yanova, A. V. Kol'tsova, Ye. S. Meyzerov, Ye. P. Kazanskaya, p. 99). However, in our experiments the second and third exposures to vibration occurred 1-2 weeks after irradiation, which could modify their effectiveness. However, there is now no basis for thinking that the phase of depression of oxidation processes was /250 absent after the second and third vibrations. It appears more probable that in the case of the repeated combined effects of vibration and irradiation on higher nervous activity the decisive role is played by some mechanisms intensifying the radiation effect or slowing down the restoration processes to such an extent that the protective effect of the oxidation processes is completely masked.

¹Reference is to G. M. Frank et al. (1965).

The masking of the role of oxidation processes in the case of combined exposure is described in the literature. A moderate physical load at the time of irradiation in a dose of 1100 r exerts a favorable effect on the course and outcome of radiation sickness in mice, despite the fact that the oxidation processes at the time of exposure to radiation should be increased for them (Shcherban', 1960).

In the literature there are indications that the radiovulnerability of the cells of the spinal cord, determined from the development of late radionecroses, has little dependence on the concentration of oxygen in the tissue. An increase of oxygen tension by a factor of 3 increases the number of late radionecroses by only a factor of 1.15 (Zeman, 1965). These data should only be used with great caution in explaining the results of our study.

Zeman investigated the dependence of radiovulnerability on oxygen stress in cerebral tissue, and L. D. Luk'yanova measured the intensity of oxidation processes. In addition, the oxygen effect and change of oxidation metabolism can act differently on radiation impairments of the structure of nervous tissue and on such a fine indicator as changes of conditioned reflexes.

The problem of the localization and mechanism of the intensifying effect of vibration on radiation effects in our experiments requires special investigation.

Conclusions

1. During the first combined exposure to 15 min vibration with a frequency of 70 cps and an amplitude of 0.4 mm and subsequent irradiation by X-radiation with 50 r, the conditioned reflex activity of rats changed in the course of six days in the same way as under the influence of vibration. Later there was a combination of the effects of both factors.

2. After the second and third combined exposures, the effects of vibration and irradiation on conditioned reflex activity, relative to the principal indices (intensity and latent periods of the conditioned reflexes), were completely summed. Dominance of the vibration effect appeared in the change of the number of phase phenomena. The relation of the changes of the conditioned reflexes to weak and strong stimuli occupied an intermediate position between the change of this index for vibrated and irradiated animals.

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